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The Journal of the Connecticut State Medical Society

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Samuel S. Engel, M.D., Guest Editor

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Interhospital Transport Audit Criteria for Helicopter Emergency Medical Services

SHERYL G.A. GABRAM, M.D., SHERRY STOHLER, R.N.,
R. KENT SARGENT, M.D., ROBERT J. SCHWARTZ, M.D., M.P.H.,
AND LENWORTH M. JACOBS, M.D., M.P.H.

ABSTRACT—A quality assurance audit of all interhospital patient transports from 17 June 1985 through 31 December 1989 by Connecticut's critical care helicopter system was performed to determine the number of medically appropriate and justified flights. There were 1,839 transports reviewed using nationally established criteria. Flights not fulfilling any of these criteria (n=401) were reviewed in detail by a panel consisting of medical and nursing representatives. During this case by case review, additional acceptable criteria for transport were developed. The audit determined that 1,792 (97%) of interhospital transfers were justified for helicopter emergency medical transport. The use of these national criteria along with the proposed additional criteria is recommended to health care personnel in the decision to transport a patient to a tertiary care hospital by air. In addition, these criteria should be prospectively utilized by aeromedical flight programs for quality assurance review of appropriateness of helicopter interhospital requests.

Introduction

CIVILIAN helicopter emergency medical programs have been in existence since 1972.[1] The evolution of these services has been from first generation programs, where single-engine helicopters transported primarily trauma patients exclusively to the helicopter sponsor's hospital, to third generation programs where twin-engine helicopters are largely used for transport of critically ill and injured patients to multiple tertiary care centers within the service region.[2] The 1990s bring the introduction of fourth generation programs, where issues of quality assurance with respect to appropriateness of patients transported and medical treatment provided are key issues.[3]

Formal helicopter emergency medical service quality assurance audits are in the developmental process.[4,5,6] The American College of Surgeons Committee on Trauma in 1983 published national indications for helicopter interhospital transports,[7] and recently the Association of Air Medical Services (AAMS) published a similar list of criteria.[8] The purpose of this study was to assess the appropriateness of helicopter interhospital utilization in an established helicopter emergency medical service based on national criteria, and to determine if other criteria should be added to the American College of Surgeons (ACS) published indications.

Methods

The critical care helicopter service of Connecticut is centrally based at Hartford Hospital, an American College of Surgeons verified Level I Trauma Center. From June 1985 through December 1989, 4,163 requests were received by the on-site despatch center with 2,894 (69.5%) missions completed. The mission statement of the program is to provide the highest level of prehospital medical care while rapidly transporting critically ill or

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Table 1

American College of Surgeons Criteria to Request Interhospital Transport by Air

TRAUMA

Central nervous system:
- Head injury with (one or more of the following)
  - Requirement for CT scan
  - Severe obtundation (GCS < 10)
  - Lateralizing signs
  - Deteriorating level of consciousness
  - Penetrating injury
  - CSF leak
  - Depressed skull fracture
  - Glasgow Coma Scale < 10 or deterioration in GCS of 2 or more

- Spinal cord injury

Chest:
- Wide superior mediastinum
- Major chest wall injury
- Cardiac injury
- Patients requiring protracted ventilation

Abdomen/Pelvis:
- Disruption of pelvic ring in two or more places
- More than five units transfusion, evidence of continued hemorrhage
- Open pelvic fracture

Combination injuries, particularly:
- Severe face injury
- Chest injury and head injury
- Abdomen or pelvis injury and head injury
- Thorax injury and abdomen injury

Secondary deterioration (late sequelae):
- Respiratory failure or sepsis in combination with late onset (24 hours) of deterioration of cardiac, hepatic, renal, or central nervous system function

BURNS

Greater than 20% total body surface
Involving the respiratory system
Involving the face, head, feet, hands, or perineum

HIGH RISK PREGNANCY where there are inadequate facilities for the mother and child.

NEONATAL CRISIS where the neonate cannot be adequately managed in the referring hospital.

CARDIAC

Myocardial infarction with cardiogenic shock where there are inadequate facilities for diagnosis and therapy.

Myocardial infarction requiring intracoronary fibrolysins.

Cardiogenic shock requiring intraaoritc ballon pump.

ACUTE MEDICAL

Acute pulmonary failure requiring sophisticated pulmonary intensive care.

Need for acute hemodialysis unavailable at referring hospital.

Neurologic emergency resulting in requirement for CT scan, severe obtundation, deteriorating level of consciousness or vital signs.

Gastrointestinal bleeding requiring angiography or other procedures unavailable at referring institution.

Severe poisonings or overdoses requiring intensive consultative care.

Complications of cancer and chemotherapy; opportunistic infections with unstable vital signs.

ORGAN TRANSPLANTATION

Any time critical situation where the speed of the helicopter may be beneficial to the recipient, eg, heart-lung, and/or liver transplantation.

injured patients to definitive care hospitals. The 150-mile service area incorporates the entire state of Connecticut.

To evaluate the mission statement of the program specifically for the group of patients transported between hospitals, a retrospective review of all completed interhospital helicopter completed transports between June 1985 and December 1989 was conducted. The American College of Surgeons (ACS) criteria for helicopter interhospital transports were used (Table 1).[7] All entries were reviewed for internal consistency by two of the three panel members. Patient transports which did not fulfill any of the ACS criteria were individually reviewed by the entire panel which consisted of the associate director of emergency medicine and trauma, the assistant medical director of the flight program, and the chief flight nurse. Additional helicopter interhospital transport criteria were developed by the panel and applied to the review process (Table 2). Three categories of transports were found to be justified: those that met ACS established criteria, those that fulfilled panel generated implicit criteria, and those that were deemed appropriate by individual case review. The panel-generated criteria were compared to the recently published AAMS guidelines for consistency.[8]

Results

A total of 1,839 flights fulfilled inclusion criteria as interhospital transports and were reviewed according to the criteria outlined above. These flights represented 63.5% of all completed missions during the time interval studied.

Applying the American College of Surgeons guidelines, 1,438 (78%) flights were justified and required no further review (Fig. 1). The remaining 401 flights (22%) were individually reviewed by the panel. Utilizing additional criteria generated by the panel with recommendations from two emergency department directors in the state of Connecticut not affiliated with the sponsoring hospital (Table 2), 342 flights (19%) were justified. These additional criteria were unanimously supported by the panel as indications for interhospital helicopter transport. To verify the panel's generated criteria, a comparison was made with the recently published AAMS guidelines for air medical transport.[8] Fourteen of the 16 criteria are recommended in the AAMS guidelines. The two panel criteria not listed in either ACS or AAMS guidelines are the need for hyperbaric decompression and hyperthermia.

The last group for justification were those that were deemed "individually" appropriate for helicopter transport. This category referred to specific instances where local resources required an aeromedical transport even in a medically stable patient. An example of this individual case justification was an adult hemodynamically stable male with a femur fracture in a hospital emergency department on a remote island with no definitive care capability and no other reasonable means of transportation. Twelve flights, less than 1%, were justified based on this individual case by case review.

Discussion

Regionalization of health care is the natural result of rising health care costs and limitation of specialized health care resources and personnel.[9] As advances in medical technology occur, the availability of these resources may be limited to tertiary care facilities. Such is the case for patients sustaining multisystem trauma, head or spinal cord injury, and burns, where treatment of such patients in trauma or burn centers has been shown to improve outcome.[10,11,12] This benefit in outcome has also been documented for neonatal, pediatric, surgical specialty, and high risk obstetrical patients.[13,14,15] The dilemma that exists relates to the transportation of this critically ill group of patients and exposing this high risk group to an out-of-hospital environment during transport.

The interhospital transport phase has limitations in equipment, performance of procedures, space, and personnel when compared to the tertiary hospital setting for managing a critically ill patient. The goal for such patient populations is to minimize this exposure. The Joint Commission for the Accreditation of Health Care Organizations (JCAHO) mandates that "a hospital is capable of instituting essential lifesaving measures and implementing emergency procedures that will minimize further compromise of the condition of any infant, child, or adult being transported."[16] It is also the transferring hospital's responsibility to ensure that the skills and equipment available during transport will provide for the needs of the patient.[17] To those ends, it is to the advantage of the transferring hospital to secure optimal transport modes, assuring that the most critically ill patient has the appropriate level of medical care and is transported rapidly to limit the out-of-hospital exposure.

Helicopter emergency medical services offer three main advantages for interhospital transport: rapid response and transport, the highest level of interhospital transport medical care available, and transport only to definitive care hospitals.[18] More than 170 hospital based helicopter emergency medical programs are in existence across the United States, verifying the enormous growth and success of such operations.[19] The larger more powerful twin-engine helicopters used in the majority of helicopter emergency medical programs travel between 140-167 mph, allowing for this rapid transport.[20]

The highest level of medical care offered by helicopter emergency medical services is reflected in the knowledge, judgment, and skills of the flight crew in addition to the equipment carried on the helicopter. In Connecticut's critical helicopter service, the flight crew consists of a pilot with a minimum of 2,000 flight hours, a flight nurse, a respiratory therapist, and on certain flights, an attending emergency medicine physician.[21,22] Flight nurses, in addition to being paramedics, have a minimum of three years of critical care experience. The education of a flight nurse consists of a three-month training program addressing the pathophysiology of disease processes, and clinical rotations through the operating room, emergency department, cardiac, surgical, neonatal, and pediatric intensive care units.[23] The respiratory therapist, trained at the EMT-Intermediate level, has a minimum of one and a half years of critical care experience and is a pediatric respiratory clinician. All physicians are certified in Advanced Cardiac and Trauma Life Support and have completed an inservice training program on prehospital management prior to flying. Advanced skills performed by the flight crew include oral and nasotracheal intubation, cricothyroidotomy, central venous cannulation,

Table 2

Additional Criteria

Trauma

1. Positive Head CT scan without definitive management capability
2. Positive Neck CT scan without definitive management capability
3. Limb injury with the need for reimplantation
4. Limb injury with the need for revascularization
5. Penetrating trauma to the neck, chest, or abdomen
6. Uncontrolled ongoing hemorrhage

Cardiac

7. Uncontrolled life threatening dysrhythmia with or without MI
8. Any unstable cardiac condition requiring urgent cardiac catheterization or cardiac surgery

Medical

9. Decompression sickness with need for hyperbaric recompression
10. Suspected dissecting thoracic aorta or ruptured abdominal aortic aneurysm
11. Severe hypothermia
12. Severe hyperthermia

Other

13. Upper airway obstruction
14. Life threatening infectious process
15. Status postcardiopulmonary arrest without definitive management capability
16. Ongoing severe metabolic acidosis without definitive management capability

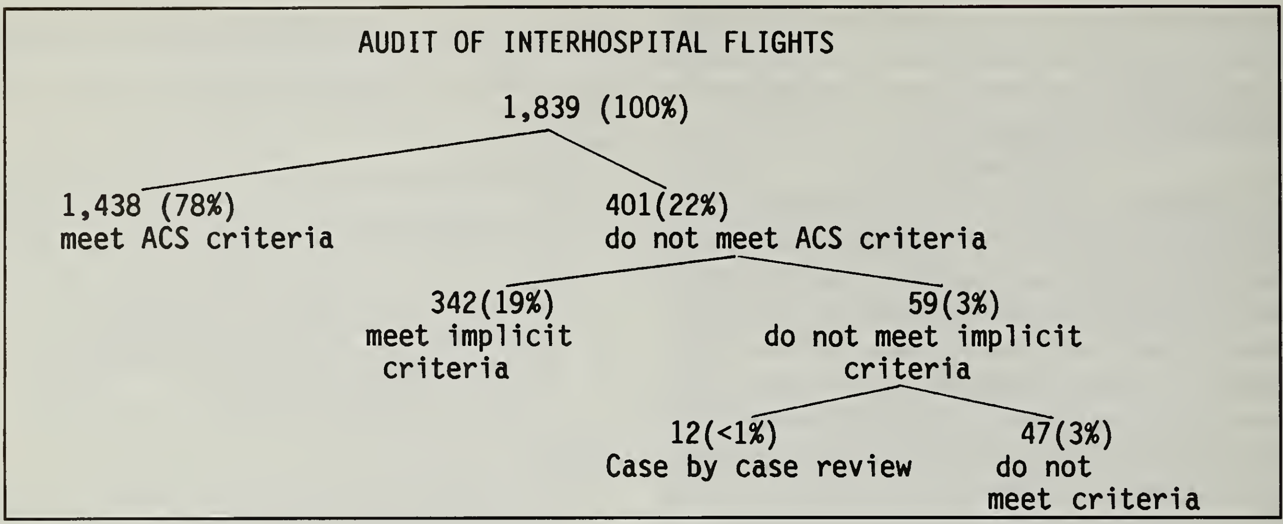

Figure 1

needle thoracostomy, chest tube insertion, intraosseous cannulation, pericardiocentesis, and escharotomy. Medications routinely carried on the helicopter include all ACLS drugs as well as paralytic medications for intubations, mannitol, dobutamine, verapamil, nitroprusside, digoxin, hydralazine, methylprednisolone, aminophylline, terbutaline, dexamethasone, oxytocin, magnesium sulfate, dimenhydrinate, and several different bronchodilator inhalers. The helicopter is equipped with sophisticated devices for precise monitoring of the critically ill patient. One of these devices is an end tidal CO_2 pulse oximeter monitor which allows for continual close monitoring of a patient's oxygenation and ventilatory status.[24] The helicopter may also be reconfigured for neonatal transports utilizing a neonatal isolette with attached pediatric ventilator. The equipment, skills, and medical expertise of the flight crew establishes this mode of transport as the highest level of interhospital medical care available in the state of Connecticut.

Because Connecticut's critical care helicopter service is such a valuable resource for interhospital transports, it is important that this resource is utilized appropriately. The purpose of this study was to identify the appropriateness of completed interhospital missions based on national criteria and to determine if a significant overutilization rate exists. Underutilization is a problem of equal importance in that patients may be denied a valuable resource. It is not measurable unless statewide data are collected. In 1986 the Task Force of the Committee on Trauma of the American College of Surgeons published a report entitled "Hospital and Prehospital Resources for Optimal Care of the Injured Patient."[7] Appendix D of that document addresses the role of a critical care air ambulance service and lists criteria to be used in requesting interhospital transportation by air. Those criteria were selected for use in this interhospital audit since they were the only nationally reported criteria available at the time of the initial review. After the time of the initial audit, the Association of Air Medical Services (AAMS), a national air ambulance organization, published air transport criteria.[8] The basis for the AAMS guidelines is a belief by the organization that air medical transport should be used when its inherent advantages over land-based transport enhance patient care. The membership of AAMS consists of medical directors of emergency departments, trauma, ground and aeromedical programs, administrative, nursing, and prehospital personnel from all parts of the country. Because of this broad representation, the AAMS criteria, published and distributed nationally, were viewed as being objective and used to evaluate retrospectively the panel-generated criteria.

A larger number of interhospital helicopter transports fulfilled the ACS criteria. Nearly all of the interhospital flights met ACS and panel-generated criteria for its own review. Recognizing this as a potential problem, the panel distributed a random sample of charts for review to two emergency department directors in the state not associated with the sponsoring hospital. The results of these comments were incorporated into generating the panel criteria. In addition, the panel-generated criteria were compared to the recently published AAMS guidelines which were not available at the time of the initial review. All of the panel-generated criteria were included in the AAMS guidelines except the need for hyperbaric treatment and hyperthermia. Hyperbaric decompression, when used to treat carbon monoxide poisoning, decompression sickness, air embolism, or clostridial myonecrosis, is time related, especially in the critically ill patient, and rapid transport to a hyperbaric chamber may influence outcome.[25] Heat stroke is a medical emergency, with mortality ranging from 25%-50%.[26] Treatment requires urgent intensive medical care, and therefore hyperthermia as defined as heat stroke should be considered an appropriate helicopter interhospital transport criterion.

A paucity of literature exists on the appropriateness of missions for helicopter emergency medical services. Williams et al reported data from a statewide helicopter utilization committee for Massachusetts reviewing 422 completed patient transports during a six-month time period.[4] A list of criteria was generated by a utilization review committee which had representation external to the two aeromedical programs studied. The committee consisted of members from the Massachusetts Medical Society, the Massachusetts Chapter of the College of Emergency Physicians, the American College of Surgeons, and the EMS community including the Massachusetts Office of Emergency Medical Services. Since this committee was organized in December 1985, many of the recommended criteria were useful to the national AAMS organization during the development of the position paper on the appropriate use of emergency air medical services. All transports, both interhospital and scene, were screened with their criteria, and those not fulfilling the criteria were individually discussed by the committee. Exceptions made by the committee in determining appropriateness included: isolated areas without teritary care facilities, for example an island, details of the mission unknown during the screening review, lack of ground service availability, and temporary intensive care unit closings. These reasons were similar to the last group of patient transports in this study that were justified by case-by-case review (n=12, Fig. 1). The total nonjustified rate of 2.4% reported in Williams study is similar to the 3% rate in this paper.

The low inappropriate call rate reported suggests either all health providers in the state are knowledgeable of the indications for interhospital aeromedical transport or, more likely, that a number of patients fulfilling the criteria are being transported by other means. In order to provide helicopter transport to the entire population that would benefit from this mode, a higher inappropriate call rate would be expected. It would be beneficial to repeat this audit after a statewide educational program on interhospital helicopter transport indications.

Conclusion

A quality assurance audit of 1,839 helicopter interhospital transports for Connecticut's critical care helicopter service revealed that 1,780 (97%) missions met established criteria. Helicopter services offer the highest level of interhospital medical care available and appropriate use of these services is important for resource utilization. During the study interval the helicopter service was not overutilized for interhospital transports. Underutilization could not be measured because of a limitation of statewide data. Nationally published interhospital helicopter indications for transport exist and should continue to be used in such quality assurance audits.[7,8]

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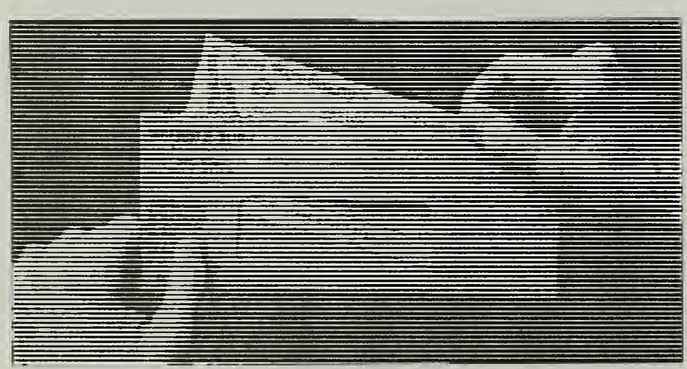

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Diagnostic Potential of Contrast MRI in Lumbar Schwannomas

VITHAL WAGLE, M.D.

ABSTRACT—Contrast enhancement in magnetic resonance imaging (MRI) is fast becoming a valuable means of diagnosing spinal pathology. The paramagnetic contrast agent, gadopentetate dimeglumine, used since 1986, delineates extradural, extramedullary intradural, as well as intramedullary lesions without myelography. However a combination of contrast MRI and water-soluble contrast myelography may prove especially useful in diagnosing mobile lesions in the lumbar region, particularly involving the cauda equina. Nerve root attachment (small spherical areas of void signal) and visualization of both the rounded cephalic and caudal ends were two other features delineated well on MRI. We report four cases of lumbar schwannomas where MRI was used alone or in conjunction with water-soluble contrast myelography to make the diagnosis.

Introduction

SCHWANNOMAS of the lumbar region and cauda equina, are slightly more prevalent than thoracic and cervical lesions.[4] Occasionally they are mobile, a feature that distinguishes them from tumors at other sites. Mobile tumors are difficult to diagnose preoperatively,[1] if a mobile lesion is suspected, water soluble contrast myelography in the standing position may confirm the diagnosis, as was the case in one of our patients.

Case Reports

*Case 1**

LPJ, a 40-year-old-female, presented with low-back pain of three months duration with left lower extremity radicular pain. There were no physical findings that would have contributed to the diagnosis. Water-soluble

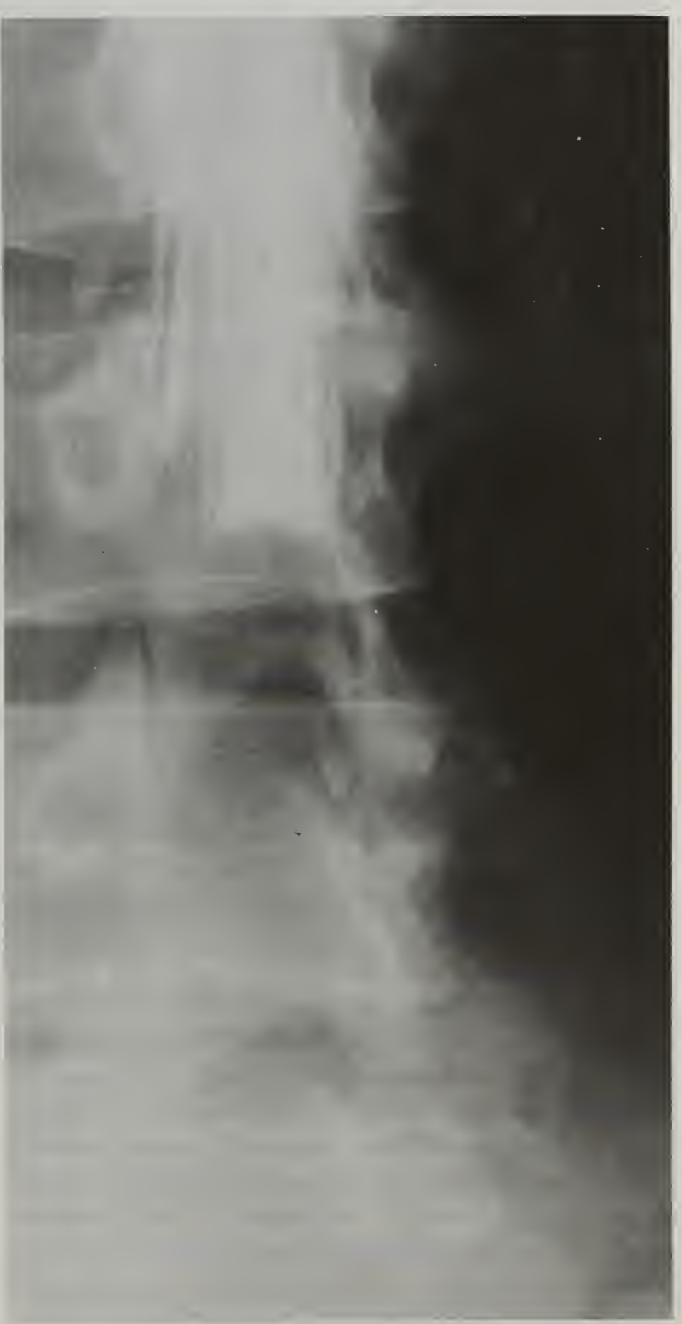

Figure 1a-b

Antero-posterior and lateral water soluble contrast myelography: Shows a complete block at upper aspect of L-4. (arrow)

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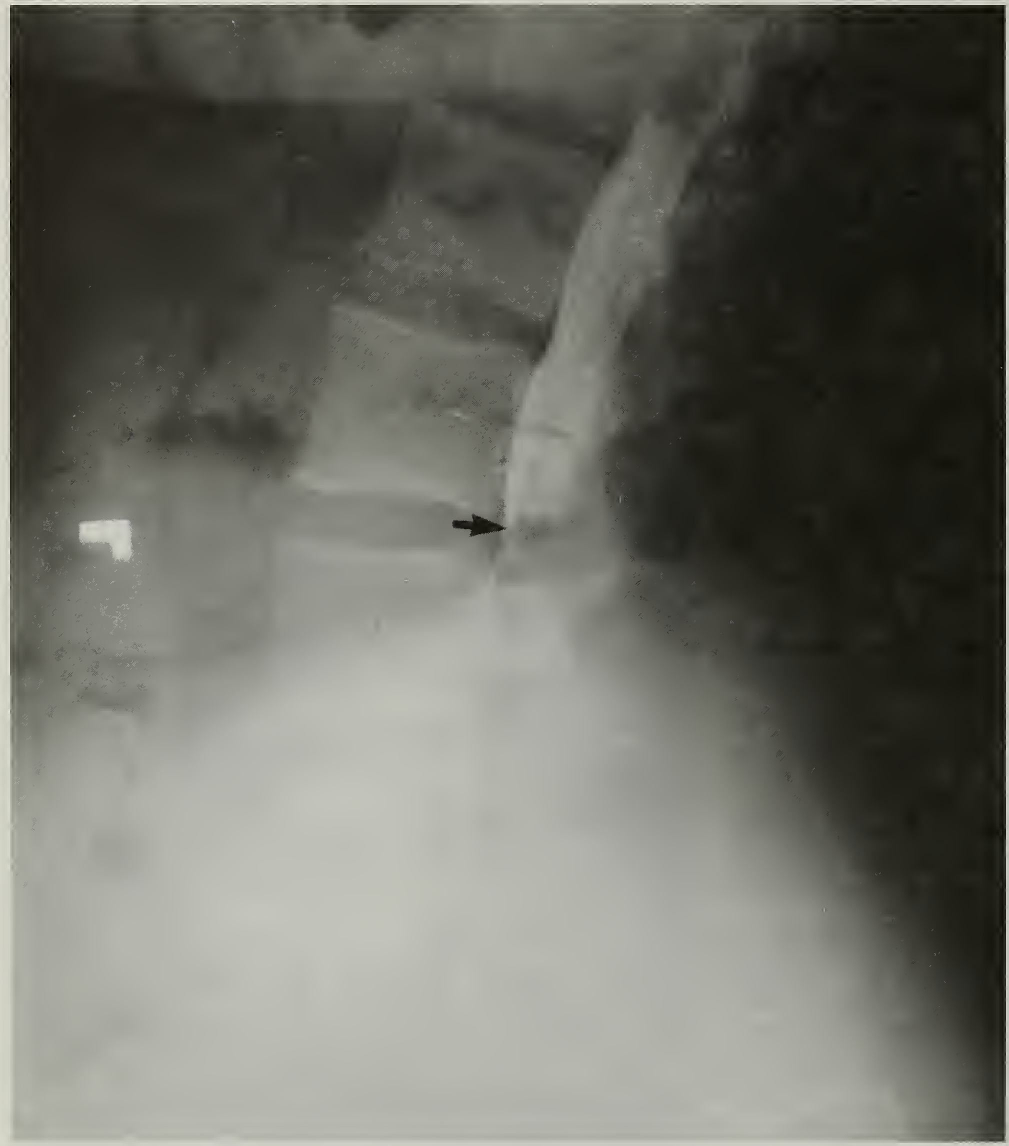

Figure 1a-b

Antero-posterior and lateral water soluble contrast myelography: Shows a complete block at upper aspect of L-4. (arrow)

contrast myelography in the standing position revealed a complete block at the upper border of L-4 (Fig. 1a-b). Cerebrospinal fluid (CSF) protein was 138 mg/dL. MRI of the thoracolumbar region was done with the spine echo (SE) technique, in the sagittal and coronal planes (GE 1.5 Telsa). The noncontrast scan was done with short and long relaxation and echo time (TR/TE 900/.20 msecs and 2000/30 msecs). Gadopentetate dimeglumine was administered and a scan done within six minutes with a TR/TE of 900/20 msecs. Noncontrast MRI demonstrated a vaguely outlined area with increased signal; in both T1 and T2 weighted images. Gadopentetate defined the cephalic and caudal ends of the tumor with clarity, at a higher level than the myelogram (L-3), suggesting a mobile lesion, probably attached to a pedicle (Fig. 2a-b). The lesion was removed through a laminectomy. The patient had no postoperative deficit due to excision of the nerve.

Case 2

ERR, a 67-year-old female, presented with right hip pain of six months duration. The pain occasionally radiated down to the right popliteal region, and was exacerbated by weight bearing. Computed tomography (without contrast) of the lumbar region, along with lumbar spine films, was normal for her age. MRI of the spine with SE technique in sagittal and axial planes with gadopentetate revealed a lesion at the cauda equina. This was initially thought to be an ependymoma because of its proximity to the conus medullaris, but other features such as rounded edges on MRI, small area of void signal at one end, distance from the conus medullaris, were clearly diagnostic of a schwannoma. Postoperative course after excision of the schwannoma was uneventful. Myelography was not performed in this instance (.3 Tesla Fonar, TR/TE 500/20 msecs).

Case 3

RFC, a 45-year-old male with a past history of Crohn's disease, presented for symptoms related to his Crohn's disease. He related a six-month history of radicular pain in the left leg, which had improved before his admission to the hospital. The improvement was possibly due to bed rest and steroids given to him when he had symptoms related to Crohn's disease. His only contributing physical finding was a restricted "Lesague" test on the left. MRI of the spine with contrast, (Fonar .3 tesla, SE, TR/TE 800/37 msecs) demonstrated a high intensity lesion overlying the body of L-5, laterally. Water-soluble contrast myelography confirmed that the lesion was intradural extramedullary. The root sleeve schwannoma was resected along with the involved root. He had no deficit following this procedure.

Case 4

GB, a 60-year-old female, living alone, was found lying on the floor of her house unable to move her legs. She was admitted to a local hospital and treated for ulcers on her legs. Noncontrast computed tomograpy of the lumbar

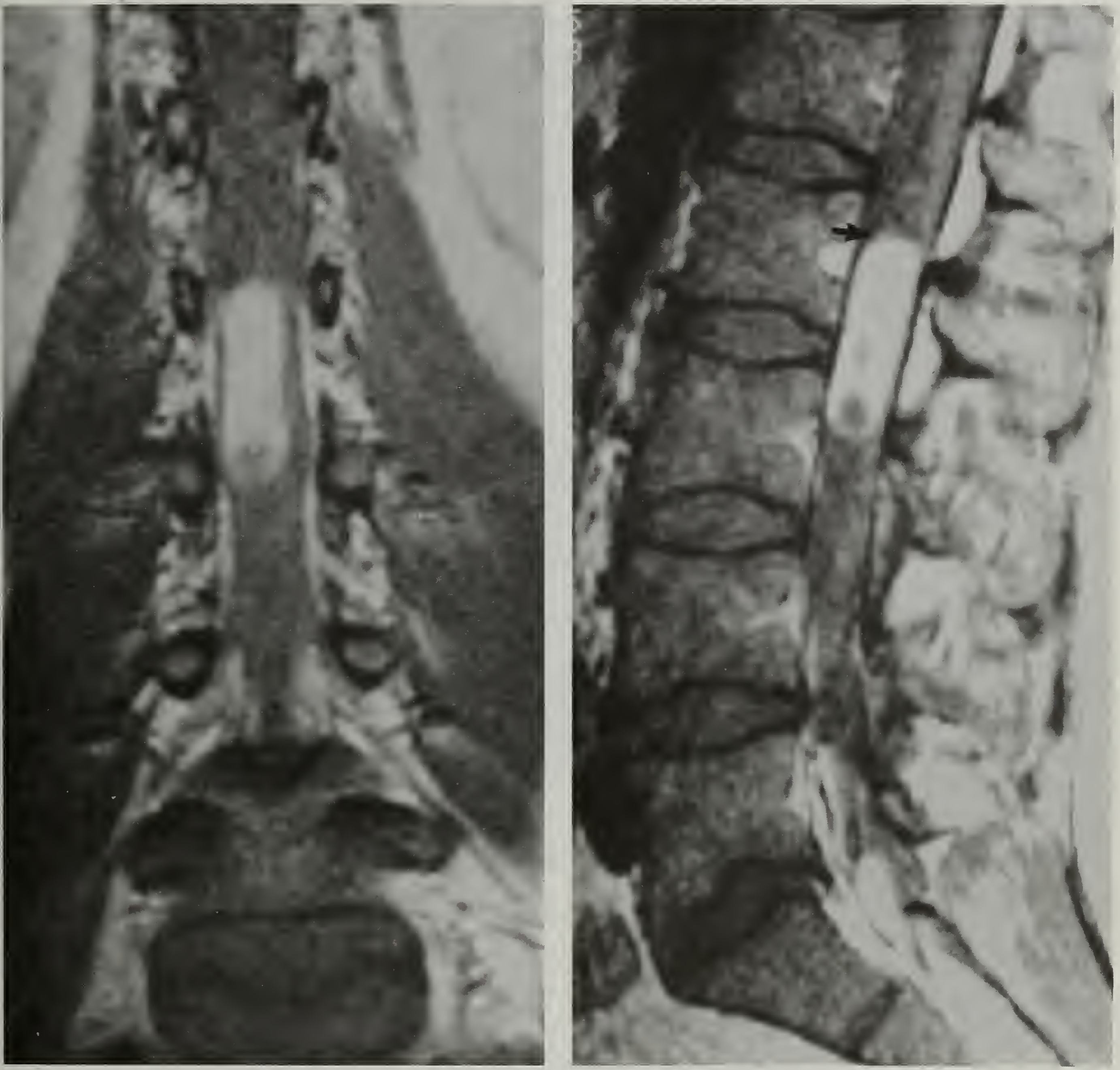

Figure 2a-b

Contrast enhanced coronal and sagittal MRI (TR 900 ms, TE 20 ms) shows the superior pole of the lesion at the midpoint of the body of L-2. Note the round signal region at the inferior pole.

spine, revealed an L 4-5 disc herniation on the left and was otherwise unremarkable. Contrast MRI of the thoracolumbar region in axial and sagittal planes, (Fonar .3 Tesla, SE technique, TR/TE 20/500 msecs) showed a lesion of the cauda equina with a small region of hypointensity at the superior aspect of the lesion.

Discussion

Schwannomas, intracranial and intraspinal, predominantly involve the sensory roots, although rarely motor roots may be involved.[4] They are distributed evenly among the lumbar, thoracic, and cervical spine. These tumors are generally intradural extramedullary; however, extradural components and infrequently tumors deeply embedded into the parenchyma are also seen.[4] Occasionally, the intrathecal component may extend through the intervertebral foramen, in an "hour-glass" fashion, into the paravertebral gutter. Meningiomas, the other common lesions of the intradural extramedullary component, as well as sarcomas and carcinomas have also been reported to have hour-glass extensions.[2,4]

Detection of mobile tumors is difficult. In our first patient (Case 1) in whom contrast MRI suggested a schwannoma, water-soluble contrast myelography was performed in the standing position. A complete block was

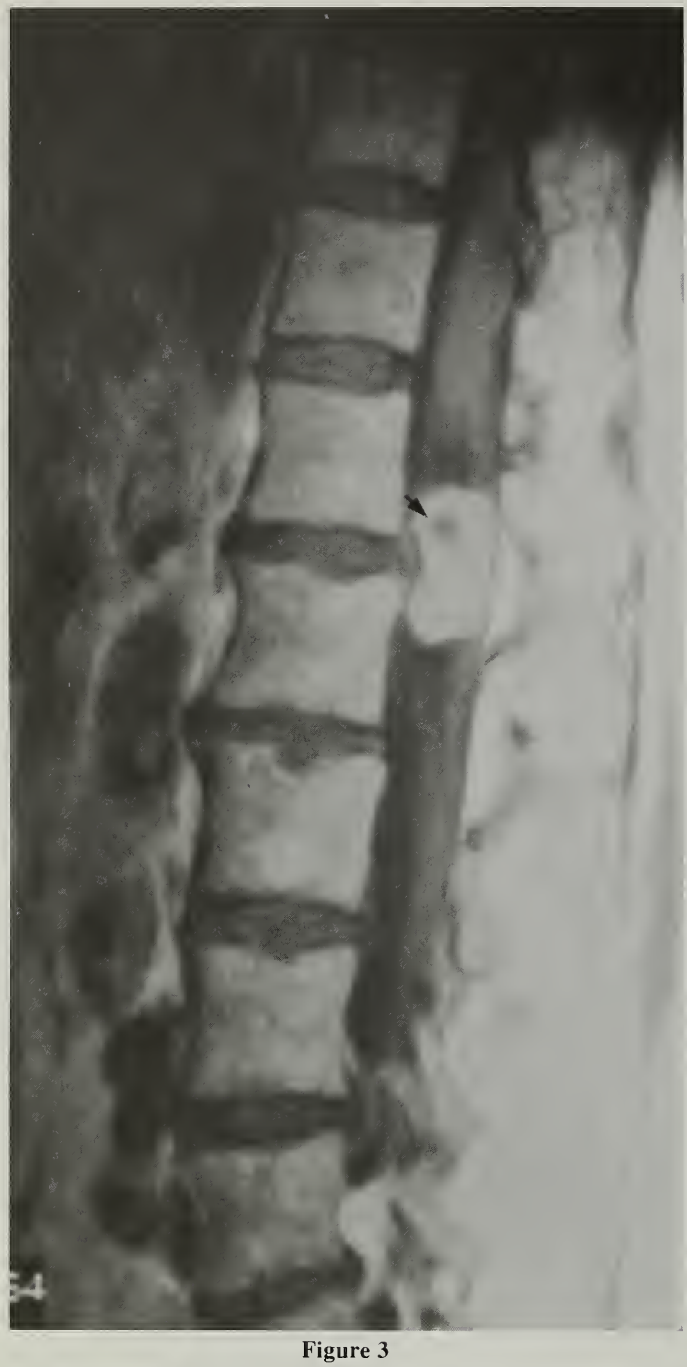

Figure 3
Sagittal contrast enhanced MRI shows the tumor between L-1 and L-2 (TR 500 ms, TE 20 ms). Note the void signal region at the superior pole (arrow).

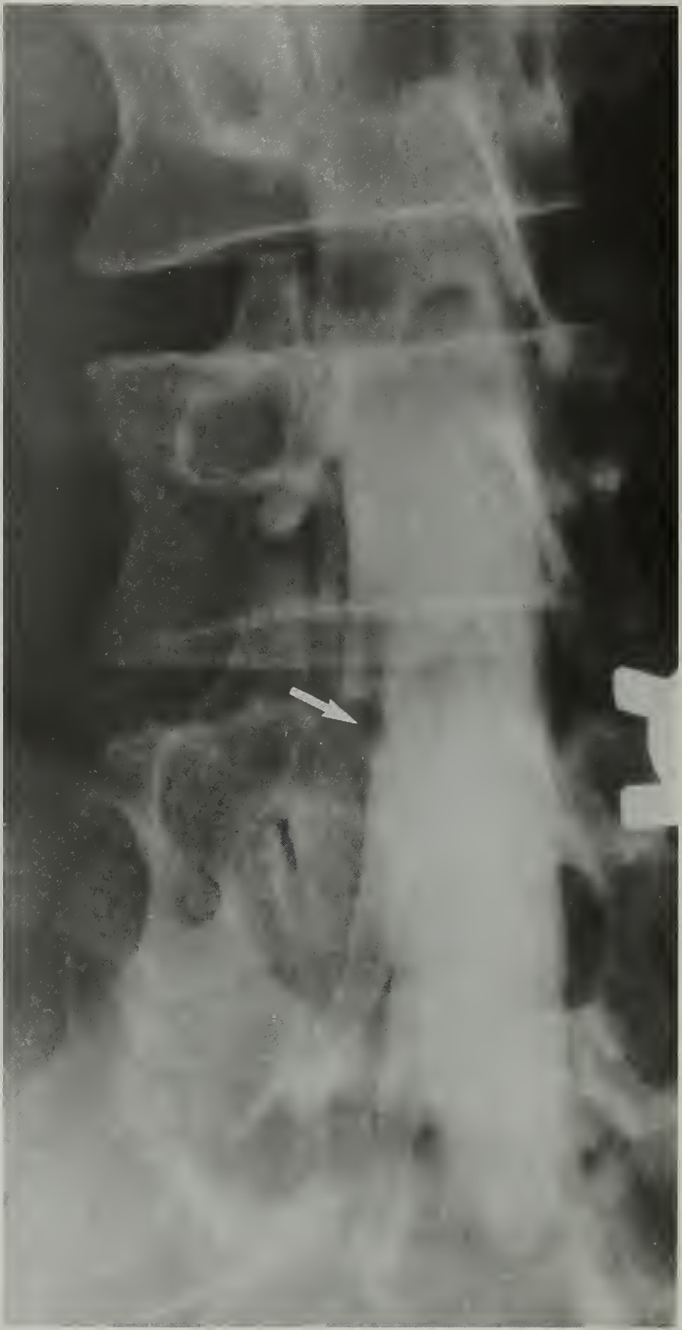

Figure 4a-b
Water soluble contrast (oblique) myelography showing a small lesion at L-5 (arrow) and axial contrast MRI shows a high intensity lesion at the intervertebral foramen on the left (TR 800 ms, TE 37 ms).

seen at the lower level than the rounded cephalic end of the tumor seen on MRI. The small area of signal void on MRI was probably the site of attachment of the nerve root seen at surgery. Preoperative knowledge of this situation allowed appropriate planning, to excise a mobile lesion.

Case 2, on the other hand, on MRI showed a lesion at L-1, which was diagnosed as an ependymoma. At the time of surgery this discrete solid lesion had pushed the nerve roots to the left, and the filum terminale was not in close proximity. The conus medullaris was identified a segment above. CSF pockets that on MRI were thought to be necrosis within the ependymoma, were partially loculated areas at both ends of the tumor and CSF here seemed under pressure. The extreme flow void, uncharacteristic of normal CSF void signal, was probably due to obstruction to CSF flow above and below the tumor, and subsequent eddying of CSF at the site because of partial blockage (Fig. 3). This effect has been reported in patients with aqueductal stenosis or other obstructive lesions. In retrospect, water-soluble contrast myelography in a standing position may have confirmed the diagnosis with a routine L3-4 puncture. In Case 3 the root sleeve

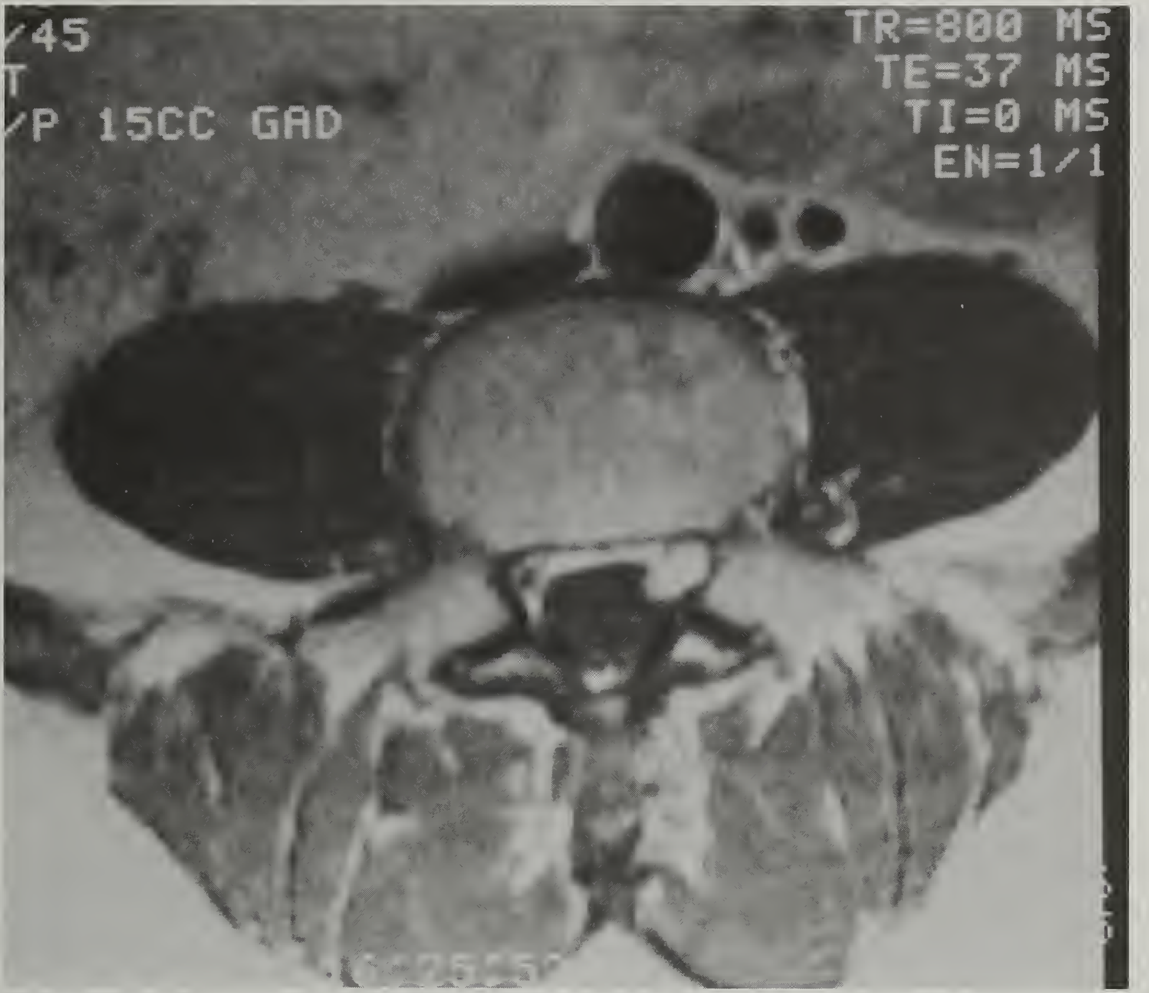

Figure 4a-b
Water soluble contrast (oblique) myelography showing a small lesion at L-5 (arrow) and axial contrast MRI shows a high intensity lesion at the intervertebral foramen on the left (TR 800 ms, TE 37 ms).

schwannoma at the intervertebral foramen was demonstrated well on MRI as well as water-soluble contrast myelography and was nonmobile (Fig 4a-b). In Case 4 an application of features encountered in the previous cases made the diagnosis relatively easy.

In summary MRI with gadopentetate dimeglumine was sufficient to make a reasonably accurate diagnosis. In combination with water-soluble contrast myelography, it was particulary helpful in diagnosing a mobile lesion. A recent study has advocated two MRI studies with a change in position.[1] In our opinion, the lateral or prone position may be difficult in obese patients; chest excursions in either of these positions might not be easy to visualize in the scanner. Preoperative awareness that the tumor is mobile is important in planning a surgical procedure. Failure to appreciate the mobility may on occasions lead to reexploration because the tumor was missed during the first surgery, or alternatively may lead to an unnecessarily extensive laminectomy. Attachment of the nerve root (seen as small round area of void signal) and visualization of both the rounded cephalic and caudal ends were the two diagnostic features demonstrated with clarity on contrast MRI. None of our patients had any neurologic deficit due to sectioning of the attached nerve root. Their other symptoms were alleviated following removal of the schwannoma.

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Important Advances in Clinical Medicine

General and Family Practice

The Scientific Board of the California Medical Association presents the following inventory of items of progress in general and family practice. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, or scholars to stay abreast of these items of progress in general and family practice that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on General and Family Practice of the California Medical Association, and the summaries were prepared under its direction.

New Guidelines to Prevent Atherosclerosis

ATHEROSCLEROTIC disease is responsible for about 700,000 deaths per year in the United States, with the majority resulting from ischemic heart disease. The National High Blood Pressure Education Program created in 1973 and the series of Surgeon General's reports on smoking issued since 1964 have raised public and professional awareness of the importance of these two particular risk factors. In a similar vein, the National Cholesterol Education Program (NCEP) was launched in 1987 with guidelines for the detection, evaluation, and treatment of hyperlipidemia. To cause a continued decline in cardiovascular mortality, the program recommends that all adults aged 20 years and older should have their total cholesterol levels measured at least once every five years. Although controversy exists about whether overall mortality is reduced by cholesterol reduction, there is a general consensus that control of this risk factor is beneficial.

Total cholesterol levels can be measured in a nonfasting person with further follow-up, including cholesterol fractionation, dependent on the total blood cholesterol level and the existence of other risk factors. Desirable blood cholesterol levels are less than 5.17 mmol per liter (200 mg per dl). Persons with cholesterol levels in the range of 5.17 to 6.18 mmol per liter (200 to 239 mg per dl) are designated as borderline high, and those with levels greater than 6.21 mmol per liter (240 mg per dl) are at high risk. Because of individual variation and laboratory inaccuracy, elevated cholesterol levels should be rechecked within eight weeks. If this level is within 0.78 mmol per liter (30 mg per dl) of the first, the average of the two levels should be used. If the second measurement is outside of this range, then a third test should be done. The average of these three becomes the patient's cholesterol level. Lipid measurements within three months of a major illness are not considered to be clinically relevant.

A careful history and physical can help detect secondary (and possibly reversible) causes of high-risk hyperlipidemias such as hypothyroidism, nephrotic syndrome, diabetes mellitus, obstructive liver disease, and cholesterol-elevating drugs, particularly progestins and anabolic steroids.

A person in the borderline-high group who has definite coronary artery disease or two risk factors, including male sex, family history of coronary artery disease, diabetes mellitus, obesity, cigarette smoking, hypertension, or a low high-density-lipoprotein (HDL) level—less than 0.91 mmol per liter (35 mg per dl)—should be considered at high risk, and decisions regarding treatment should be based on a fasting lipoprotein analysis that measures actual levels of low-density lipoproteins (LDLs) and HDL levels. Using these cutoff points, 25% of the adult population will have a cholesterol level in the high range (total cholesterol greater than 5.21 mmol per liter or LDL level greater than 4.13 mmol per liter [160 mg per dl]).

Dietary therapy using the American Heart Association (AHA) step I diet consists of 30% or less of calories from fat, including less than 10% of total calories from satu-

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rated fatty acids, and a cholesterol intake of less than 7.76 mmol per liter (300 mg per dl). If three months on this regimen does not lower cholesterol levels adequately, the AHA step II diet should be considered, which further reduces saturated fats to less than 7% of total calories and cholesterol to less than 200 mg per day. If these persons are unable to bring their level into a normal range despite six months of dietary therapy, then drug therapy should be considered.

With the aggressive reduction of cholesterol levels, there is a potential not only to halt atherosclerotic lesion formation but also to possibly regress the size of existing plaques.

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Expert Panel: Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *Arch Intern Med* 1988; 148:36-69.

New Guidelines for Tuberculin Skin Test Interpretation

UNTIL 1983, the incidence of active tuberculosis in the United States had been decreasing steadily. Since then it has been increasing. Today a high incidence is reported among recent immigrants from the third world; other ethnic minority populations, especially African Americans, Hispanics, and Native Americans; those infected with the human immunodeficiency virus (HIV); and elderly residents of long-term-care facilities.

The best way to identify persons infected with tubercle bacilli is the intradermal purified protein derivative (PPD) skin test. The tuberculin skin test is one of the oldest medical technologies still in daily use. Tuberculin was first derived by Koch in 1890; Mantoux, a French physician, developed the intradermal skin test in 1908; and purified protein derivative of tuberculin was first produced in 1934. Despite 50 years of research, there still is no better screening test for determining who has been infected and, therefore, who is at risk for active tuberculosis developing.

Unfortunately, the cross reactivity of the skin test with nontuberculous mycobacterial exposure frequently results in positive test in those who come from areas of high nontuberculous mycobacterial prevalence—such as southern United States—or in those who have had a bacille Calmette Guérin (BCG) vaccination, which is still used in many Asian and Central and South American countries. The size of this reaction is usually from 10 to 15 mm of induration but may be boosted by repeated testing. On the other hand, using 10 mm as a cutoff point may give false-negative interpretations in situations where it is important to offer preventive therapy—such as those recently infected or who are HIV-positive.

These factors have prompted the Centers for Disease Control's (CDC's) Advisory Committee for the Elimination of Tuberculosis to change the criteria for recommending isoniazid preventive therapy. These new criteria, based on age, incidence, and risk factors, are given in Table 1.

The two key changes are the recommendation that a PPD result of 5 mm or more of induration is a positive test in populations with risk factors for *Mycobacterium tuberculosis* infection and that a PPD reaction must be 15 mm or more to be interpreted as positive in those at low risk. This latter change is to avoid false-positive interpretations and to minimize potentially inappropriate preventive therapy.

Regardless of the CDC's criteria changes, isoniazid preventive therapy (300 mg per day for 6 to 12 months) works. It will prevent the development of active tuberculosis in those infected, both while they take it and for many years (if not a lifetime) thereafter. The widespread

TABLE 1.—*Criteria for Determining the Need for Preventive Therapy*

Category	*Age < 35 Years*	*Age ≥ 35 Years*
No risk factor, low-incidence group	Treat if PPD ≥ 15 mm	Do not treat
No risk factor, high-incidence group[†]	Treat if PPD ≥ 10 mm	Do not treat
Risk factor[*] present, either incidence group	Treat all ages if PPD ≥ 5 mm and has HIV infection, recent contact with infectious person, or fibrotic lesions on chest radiograph	
	Treat all ages if PPD ≥ 10 mm and there is recent tuberculin skin test conversion (≥ 10 mm increase for those younger than 35; ≥ 15 mm increase for those 35 years and older); intravenous drug use; or patient has medical conditions that may increase risk of tuberculosis	

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[*] Risk factors include HIV infection, recent contact with infectious person, fibrotic lesion on chest radiograph, recent tuberculin skin test conversion, intravenous drug use, or the presence of medical conditions that may increase the risk of tuberculosis, such as diabetes mellitus, silicosis, immunosuppression, or malnutrition.

[†] High-incidence group includes foreign-born persons from high-prevalence countries, African Americans, Hispanics, Native Americans, and residents of long-term-care facilities and correctional institutions.

and continued use of preventive therapy is our best hope of again decreasing the number of persons with active tuberculosis in the United States.

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Zidovudine in the Treatment of Human Immunodeficiency Virus Disease

THE treatment of human immunodeficiency virus (HIV) disease initially consisted of antimicrobial therapy for the opportunistic infections associated with the acquired immunodeficiency syndrome (AIDS). More recent research has been directed at developing a means of controlling the progression of infection by the virus itself. Zidovudine (AZT) is a thymidine analogue that inhibits HIV viral replication by interfering with the function of the viral reverse transcriptase.

Researchers reported the results of a placebo-controlled trial of zidovudine in adults with AIDS or severe AIDS-related complex. At a dose of 1,500 mg of zidovudine per day, there was a statistically significant decrease in mortality and the frequency of severe opportunistic infections that persisted for 18 months. Hematologic side effects were seen and included severe anemia and neutropenia.

The recent AIDS Clinical Trail Group Study examined the use of zidovudine in symptomatic adults infected with HIV who had a CD4 cell count below 0.5 x 10^9 per liter (500 per µl). People were assigned to one of three treatment groups: those receiving placebo, 500 mg of zidovudine per day, or 1,500 mg of zidovudine per day. There was significantly less progression to AIDS or advanced AIDS-related complex in the two zidovudine treatment groups compared with the placebo group. There was no advantage to the higher dose of zidovudine in preventing the progression of HIV disease. The high-dose zidovudine group had the known hematologic side effects of anemia and neutropenia. These were not seen in the low-dose or placebo groups. The only side effect that was unique to the low-dose zidovudine group was nausea. The use of zidovudine in HIV-infected persons with CD4 counts greater than 0.5 x 10^9 per liter is under investigation.

These are important clinical findings in light of the fact that most HIV-infected persons are currently asymptomatic. Primary care providers are in the position to identify persons who may benefit from the prophylactic use of zidovudine by offering HIV testing to their patients. The Food and Drug Administration has recently approved the use of zidovudine therapy (500 mg per day in five 100-mg doses) in persons with CD4 cell counts below 0.5 x 10^9 per liter. Patients receiving 500 mg per day of zidovudine should be monitored monthly with complete blood counts. Hemoglobin levels of less than 4.96 mmol per liter (8 grams per dl) or neutropenia, or both, indicate serious hematologic complications and may require discontinuation of the medication or a reduction in medication dose.

Questions remain regarding the long-term use of prophylactic zidovudine. The long-term side effects, the impact on survival, and the clinical significance of possible drug resistance are not known. Despite these uncertainties and the relatively high cost of zidovudine therapy, the minimal side effects with a 500-mg-per-day dose and the apparent delay in disease progression to AIDS make the use of zidovudine prophylaxis a serious consideration for asymptomatic HIV-infected persons with CD4 lymphocyte counts below 0.5 x 10^9 per liter.

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Advances of the United States Preventive Services Task Force in Health Promotion and Disease Prevention

HEALTH promotion and disease prevention are important aspects of family practice. Over the years, many opinions and recommended guidelines have been promulgated, but it has always been left up to individual practitioners to decide which interventions to use. In 1984 the U.S. Department of Health and Human Services convened a special working group, the U.S. Preventive Services Task Force. This group worked collaboratively with the Canadian Task Force on the Periodic Health Examination, which had previously done extensive work in the area. The result of this collaborative effort is the first set of truly comprehensive guidelines on the subject: the *Report of the U.S. Preventive Services Task Force: Guide to Clinical Preventive Services.*

This guide synthesizes four years of extensive review of existing medical literature and interviews with numerous experts on preventive services. It contains recommendations on 169 screening, counseling, and immunization interventions for the prevention of 60 different common illnesses and conditions. Among the topics covered are cholesterol, coronary artery disease, breast and other cancers, prenatal disorders, nutrition, low back injury, dental disease, childhood and adult immunizations, chemoprophylaxis after exposure to various infections, smoking, alcohol abuse, and motor vehicle injuries.

The scientific basis for each intervention is evaluated in the following areas: "burden of suffering" (incidence prevalence, morbidity, and mortality); "efficacy of screening tests" (sensitivity, specificity, predictive value, and reproducibility); and "effectiveness of early detection" (availability of "clinical interventions which can prevent or delay progression of the disorder"). For example, in the area of colorectal cancer, the task force neither endorses nor discourages screening, noting that despite the high burden of suffering, the efficacy of available screening methods is suboptimal and the effectiveness of early detection is not conclusively proved. It recommends screening for high-risk persons.

In other controversial areas, the task force also takes a middle-of-the-road position. In contrast to the 1988 recommendations of the National Cholesterol Education Program Expert Panel in which cholesterol screening is recommended every five years for all adults older than 20 years, the task force's recommendation is for "periodic screening" of middle-aged men. The task force mentions the expert panel's recommended frequency of every five years and states that it may be "clinically prudent" to screen others as well. The task force's "suggested threshold" for drug therapy is higher than the 1988 panel's recommendations, namely, a cholesterol level of 6.21 mmol per liter (240 mg per dl) in high-risk patients and 6.85 mmol per liter (265 mg per dl) in patients with no risk factors, versus 5.17 mmol per liter (200 mg per dl) and 6.21 mmol per liter, respectively. The task force's reasoning is that the effect on coronary artery disease of drug therapy in persons other than middle-aged men with levels of 6.60 to 6.85 mmol per liter (255 to 265 mg per dl) has not yet been proved; therefore, the potential risks and costs are not justified.

In the area of breast cancer screening, the task force's recommendations are also slightly different from previously published guidelines. In contrast to the 1987 and 1988 recommendations of the American Cancer Society and the National Cancer Institute, the task force recommends annual breast examination for all women beginning at age 40 and mammography every one to two years beginning at age 50. The recommendations for Pap testing is similar to the 1988 consensus statement adopted by the American Cancer Society, the American Academy of Family Physicians, and others, except for the addition of a recommended discontinuation at age 65 in women with previously normal Pap smears.

The recommended use of all of the interventions is summarized in a series of tables grouped according to age, sex, and other risk factors. Each table is appended with footnotes that detail the high-risk conditions for which certain interventions should be applied. Also listed in each table are the leading causes of death for each group, such as motor vehicle crashes, homicide, and suicide in teenagers; additional preventive services to be considered; and items to "remain alert for"—such as depression, abuse and neglect, and dental disease in the elderly.

Several important conclusions and implications emerged from the task force's review of existing evidence. First is that the most important contributors to preventable morbidity and mortality are the personal health behaviors of smoking, alcohol use, poor nutrition, and physical inactivity. The implications of this is that interventions which address these behaviors, namely counseling and patient education, may have a more valuable effect than conventional ordering of tests. Further, as the locus of responsibility for personal health practices necessarily shifts onto patients, physicians will need to use appropriate communication skills to help empower patients to change their behaviors.

Finally, the task force's review pointed out the inadequacy of existing data. Either studies were completely lacking in some areas, or existing studies were nonconclusive due to improper study design. This points out a vital area of research in which family practice could make a significant difference. The task force guide can be obtained by calling 1-800-638-0672 and asking for publication No. 97913-0.

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Pap Smear Update—The Bethesda (Nomenclature) System

THE Papnicolaou smear deserves credit for the significant decline in the incidence of invasive cervical cancer in screened populations. Despite the wide adoption of this screening tool in the United States since its introduction in the 1940s, however, 7,000 women per year continue to die of this theoretically preventable disease. Related Pap smear issues currently being studied and reported in the literature include risk factors for cervical carcinoma (including human papillomavirus); the cost-effective frequency of screening (the U.S. recommendation for every one to three years is related to risk factors and personal Pap smear history); improving the access to screening for low-income, high-risk populations; specimen collection techniques, such as cytobrush for nonpregnant endocervical cell sampling; laboratory quality assurance, including uniform and clinically relevant interpretation and reporting of results; and the appropriate clinical management of inadequate and abnormal specimens.

In December 1988, the National Cancer Institute convened 51 experts from the disciplines of pathology, cytology, and obstetrics and gynecology in Bethesda, Maryland, to address the last two issues. The participants unanimously agreed to view the Pap smear report as a medical consultation (improved by adequate clinical data) and to adopt the Bethesda System as the preferred nomenclature for cervical and vaginal cytopathology reporting.

The Bethesda System introduces two new, inclusive, descriptive terms: *low-grade* and *high-grade squamous intraepithelial lesion*. Previous nomenclatures, felt to be nonspecific and not reproducible, have been absorbed into the two larger categories. Low-grade squamous epithelial lesion is the new designation for the former mild dysplasia, cervical intraepithelial neoplasm, or CIN 1, and cellular changes associated with human papillomavirus. High-grade squamous epithelial lesion encompasses *moderate dysplasia* to *carcinoma in situ*, or CIN 2 to CIN 3. Atypia is now used to describe only changes of undetermined significance—that is, not inflammation.

The new report format would include the following:

- A statement of specimen adequacy—satisfactory, less than optimal, or unsatisfactory;
- A general categorization of diagnosis—within normal limits or other—to facilitate clinical triage; and
- A descriptive diagnosis—infection and type, reactive or reparative changes, epithelial cell abnormalities, nonepithelial malignancy, hormonal evaluation, or other.

When results are not within normal limits, or when specimens are unsatisfactory, the report should include clinical recommendations for follow-up by the reporting cytologist.

The Bethesda System attempts to clarify the Pap smear screening diagnosis and to exploit the consultant role of the cytologist. The objective is to facilitate the appropriate clinical investigation and early intervention for which Pap smear screening is intended.

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Nonpharmacologic Management of Hypertension

MUCH of the impetus for promoting nondrug approaches to control blood pressure stems from the risks associated with medication use, especially among mildly hypertensive patients. This also presents an opportunity to modify associated risk factors in susceptible persons. The 1988 Report of the Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure recommended that nonpharmacologic approaches be used both as definitive intervention and as an adjunct to drug therapy.

The recommendation to reduce sodium intake has become a practice standard for blood pressure control. The average American diet contains about 10 to 20 grams of salt per day (170 to 350 mEq of sodium). Moderate sodium restriction has been shown to reduce systolic blood pressure by an average of about 10 mm of mercury and the diastolic pressure by about 5 mm of mercury. It is important t note that the effect of this restriction is not universal. Some patients—for example, African Americans and elderly—are more salt-sensitive than others.

The incidence of hypertension among obese persons is 50% greater than among those with normal body weight. In past studies, weight loss has resulted in a substantial lowering of blood pressure.

Controversy exists regarding the role of low levels of potassium, magnesium, and calcium in the development and maintenance of hypertension. Nevertheless, it would be prudent to maintain adequate levels of these important cations.

Vegetarians and persons with a diet high in polyunsaturated fats have been shown to have lower blood pressures than those with a diet high in saturated fats and low in polyunsaturated fats. Recently it was shown that ingesting 50 ml of fish oils per day for two months resulted in an average decline of 6.5 mm of mercury systolic and 4.5 mm of mercury diastolic blood pressure in hypertensive persons. These studies provide further impetus for recommending a heart-healthy diet.

Because ingesting more than 1 oz of alcohol per day may be responsible for a large percentage of hypertensive patients seen in family practice, limiting alcohol intake is an important recommendation.

The direct benefits of exercise on blood pressure control are difficult to isolate from those of the changes that often accompany exercise, such as improved diet, weight loss, and decreased cigarette smoking. Considerable evidence suggests, however, that regular aerobic exercise by itself does effectively reduce blood pressure. Declines in mean diastolic blood pressure from 117 to 97 mm of mercury have been documented after just three months of daily walking or running 3 km (2 mi).

Life-style changes should be encouraged to forestall, minimize, or obviate the need for medication. One study showed that by reducing weight, salt, and alcohol intake, 39% of patients with less severe hypertension previously controlled with medication remained normotensive for four years without requiring any medication.

Using a nonpharmacologic approach to hypertension is an important adjunct for controlling blood pressure. Benefits may include not only reducing the need for medication, but also improving the subjective perception of well-being and increasing quality of life. It is important, however, to monitor the progress of patients placed on a nondrug regimen. If the diastolic blood pressure remains above 90 mm of mercury after employing nonpharmacologic measures for at least six months, then drug therapy should also be considered.

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A New Treatment of Nocturnal Enuresis

ALTHOUGH 2 to 3 million children nationwide suffer some degree of distress because of nocturnal enuresis (bed wetting), there continues to be controversy as to its origin and treatment. Enuresis is defined as a lack of bladder control in a child who has reached an age when urinary control is usually expected. Although most children have achieved control by four years of age, some 10% of six-year-old children and 2% of 14-year-olds have nocturnal enuresis. There is evidence that heredity plays a role, but separating genetic characteristics from family expectations is difficult. The differential diagnosis includes infection, neurogenic urinary bladder, diabetes mellitus, urinary tract anomalies, and emotional problems. Enuresis is primary if bladder control has never been completely present and secondary if urinary incontinence has not occurred for a prolonged period (six months or more). While secondary enuresis is likely to be associated with an underlying illness, infection, or psychosocial stress, the overwhelming majority of cases of primary enuresis are not associated with any of the forementioned causes.

Although studies show that the functional bladder capacity of enuretic children is smaller than that of nonenuretic children, their daytime bladder function is basically normal. Thus, the role of functional capacity is unclear. Conventional therapies for children affected with nocturnal enuresis include setting alarm clocks to awaken the child to go to the bathroom, a regimen of imipramine hydrochloride, and moisture alarms. Unfortunately, some children are only partially helped, and results are less than satisfying to physicians, patients, and parents alike.

Recent studies in Denmark indicate that enuresis may be directly related to an insufficient secretion of antidiuretic hormone (ADH) at night, resulting in a nighttime overproduction of urine. Normal children were found to regulate urine production by increasing ADH levels at night. Enuretic children, however, did not have an increase in ADH levels and produced an abnormally large volume of urine that resulted in bed wetting. Enuretic children were also found to urinate with a full bladder, and, in some cases, were found to repeatedly fill their bladder throughout the night. Having identified these striking physiologic changes in enuretic children, researchers successfully used desmopressin acetate nasal spray (DDAVP), a synthetic ADH, to decrease urine output and stop the enuresis. These early studies led to subsequent well-controlled, double-blind clinical trials that have confirmed that DDAVP is effective in controlling night-time urine production.

Desmopression acetate is currently available in a nasal spray pump and has been approved by the U.S. Food and Drug Administration for the treatment of primary nocturnal enuresis. The nasal spray is applied directly to the nasal mucosa, and the dosage should be adjusted according to the individual response. The recommended initial dose for children who are six years of age and older is 20 μg (0.2 ml solution) at bedtime, though some patients may respond to less medication. Adjustments up to 40 μg are suggested if there is no response. The manufacturer recommends that half of the dose be administered in each nostril. Side effects are usually mild and are limited to mucosal irritation, with occasional dose-related gastrointestinal upset. Serum electrolyte levels should be checked if therapy is continued beyond seven days.

Although patients have been kept on the medication therapy for extended periods of time, no adequately controlled studies with intranasal DDAVP in primary nocturnal enuresis have been conducted beyond four to eight weeks. The high cost of the medication (more than $60 per month) is a limiting factor to a widespread application of this treatment approach. At the same time, the fact that many people are willing to pay this much for the medication underscores the level of emotional distress that some patients and families experience as a result of nocturnal enuresis.

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Progestin-Only Contraception

PROGESTIN-ONLY contraceptive methods work by altering the cervical mucus, making it thick and scanty so that it is more difficult for sperm to penetrate; by affecting motility of the oviduct and uterus, thus affecting ova and sperm transport; and by altering the endometrium so that less glycogen is available for blastocyst survival. Ovulation may be inhibited as infrequently as 10% of the time. The progestin-only pill, used in England for years, has a failure rate of 1% to 2.5%. Although intermittent irregular bleeding is a frequent side effect, the progestin-only pill is especially useful for a woman who is breastfeeding or who has estrogen-related side effects, such as cholasma, using the combined pill. Injectable progesterone is used worldwide, but its use has not been approved in the United States, primarily because mammary tumors developed in beagle dogs during experimental testing; this work is being repeated. Vaginal rings and intrauterine devices that release progesterone have also been developed.

Recently approved by the Food and Drug Administration is the levonorgestrel implant, Norplant, which releases 50 to 80 μg of levonorgestrel daily in the first year, then 30 to 35 μg in subsequent years. With this progestin-only method, ovulation is inhibited in at least 50% of cycles. Using a trochar, six matchstick-size silastic capsules are placed under the skin of the upper inner arm. It is effective for five years and has a 98.5% effectiveness rate. Side effects include irregular menstrual bleeding (60% to 70%) and headaches (5% to 20%). Placement takes about 15 minutes and is easier than removal because over time, fat and fibrous tissue can develop around the capsules. A new system, Norplant-2, is being developed that would use only two capsules, provide the same efficacy, last for three years, and, because of requiring fewer capsules, be easier to insert and remove. It is likely that Norplant will soon be replaced by Norplant-2.

Next on the horizon is a biodegradable progestin-only implant. One form will be norethindrone in cholesterol. It is not clear how easy these will be to remove in a patient with severe bleeding or if a patient requests removal. In fact, recent data indicate that it will not be possible to remove them.

There are several question and concerns with the progestin-only methods. One is the common side effect of irregular bleeding, which leads 12% to 19% of women to discontinue the levonorgestrel implant. Levonorgestrel is one of the more androgenic progestins currently marketed in the United States, and, although the capsules release a low dose, the potential may exist for side effects such as those seen with androgenic progestins in the oral contraceptive pill, for instance, acne, hirsutism, and depression. Clinical trials have shown an incidence of acne of 5% to 20% and have not reported the other side effects. Although initial trials of the levonorgestrel implant have demonstrated a drop of 5% to 15% of both high-density liproprotein (HDL) and low-density lipoprotein (LDL) levels, longer term studies of its effect on lipids will be necessary because it is known that the progestin component of the combined pill tends to increase LDL levels and decrease HDL levels. Finally, recent studies in macaque monkeys show that progestin-only contraception was more likely to cause atherosclerosis than balanced estrogen-progestin contraception.

On the one hand, the levonorgestrel implant will be a useful method for women who find it difficult to comply with other contraceptive options, and who want an effective method. On the other hand, side effects may lead many women to have them removed.

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Pregnancy Testing—Home and Office

THE rapidly changing technology for pregnancy tests has greatly enhanced our ability to confirm early pregnancy not only in the office or laboratory setting but also in the home. Home pregnancy tests were first marketed in the 1970s, and they have been increasingly accepted (used by about 30% of pregnant women) despite concern regarding their accuracy. The first home pregnancy test, "ept," did not require Food and Drug Administration (FDA) approval. The FDA has judged all subsequent products to be "substantially equivalent," thus free from regulation. While manufacturers claim 98% to 99% accuracy as early as six days after the missed menses, one study resulted in a positive predictive value of only 65.5% for pregnancies of nine days or less from the missed menses.

Until recently, most office pregnancy tests were latex agglutination inhibition tests or hemagglutination inhibition tests (performed using either slide or tube techniques). These have generally been replaced by monoclonal antibody tests, which are more sensitive and specific. Latex agglutination inhibition slide tests are positive with human chorionic gonadotropin (hCG) levels of 1,500 to 3,500 IU per liter 38 to 42 days after the last menstrual period. Latex agglutination and hemagglutination inhibition tube tests are slightly more sensitive, turning positive with hCG levels of 750 to 850 IU per liter 35 days after the last menstrual period.

Monoclonal antibody tests are far more sensitive, turning positive with hCG levels of 20 to 50 IU per liter 24 to 27 days after the last menstrual period. Urine is placed on a membrane with anti-α monoclonal antibodies; hCG in the urine binds to the membrane. A solution is added that reacts with the ß-subunit, creating an antibody-hCG-antibody complex. This second antibody attaches to the complex, creating a blue dot, which indicates a positive test. While monoclonal antibody tests are usually done using urine, they are also available using serum (accurate even with hCG concentrations as low as 10 IU per liter). An extra step is required to achieve this small increase in sensitivity, which is seldom of clinical relevance compared with urine tests.

The percentage of positive tests at 13 days and 16 days after ovulation (documented by ultrasonography) or follicular aspiration is 75% and 100%, respectively, for "FACT," 60% and 75% for "Daisy 2," and 95% and 95% for "Advance." FACT and Daisy 2 use monoclonal antibodies that detect hCG in urine with a hemagglutination inhibition assay. Advance uses monoclonal antibodies that assist enzymes specifically to detect hCG.

The reliability of any test depends on the experience and competence of the user. Home tests have been significantly more accurate when used by older patients or those with higher incomes. The false-negative rate when used at a family planning clinic is lower (16.7%) than when used in a private office (21.1%) or a general public clinic (40.0%).

Monoclonal antibody testing now available for home and office will assist in earlier diagnosis. To improve accuracy, unless medically imperative, patients should be encouraged to wait longer than the six to nine days after the missed menstrual period that manufacturers recommend. Patients must be instructed in the proper technique, including the use of a morning's first urine. When used appropriately, home pregnancy tests enable patients to take increased responsibility for their own health care and minimize potential risks, such as exposure to drugs or irradiation during early pregnancy.

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Immunization Update

MANY revised recommendations for routine immunizations for children, adults, and certain high-risk groups have been published recently. For example, there are two new immunizations for children, and the schedule for routine immunizations has changed. The recent measles epidemic stimulated new recommendations for immunizing adults against measles. There are also new recommendations for certain high-risk groups, such as health care workers and patients with human immunodeficiency virus (HIV) infection.

Children

Originally the *Haemophilus influenzae* type b (Hib) vaccine was recommended for high-risk children at 18 months and all other children at two years of age. One *H influenzae* b conjugate vaccine (HibTITER, Lederle) is now available. This new immunization should be given at the two-, four-, and six-month visits (with oral attenuated poliovirus vaccine [OPV] and diphtheria and tetanus toxoids with pertussis vaccine [DTP]) with a booster at 15 months. Prophylactic acetaminophen administration decreases the systemic side effects of the DTP immunization in children. Other conjugated vaccines may soon be shown to be safe and effective for administration before 15 months of age. Measles immunization continues to be given in combination with mumps and rubella (MMR). Until recently they were given only at 15 months, but now they are given at both 15 months and four to six years. In recent areas of high risk, the MMR-1 should be given at 12 months of age. finally, the six-month dose of OPV can now be dropped in low-risk areas.

Adults

The influenza vaccine continues as a standard of medical practice to be considered for those with severe medical conditions (especially heart and lung disease), those older than 65, nursing home residents, immunocompromised patients (including people with the acquired immunodeficiency syndrome), and health care workers. All adults older than 65 years and patients with certain chronic medical conditions should receive the pneumococcal vaccine one time. Recent reports that at least 40% of persons 60 years of age and older are not adequately immunized against diphtheria and tetanus should lead to an increased use of the dT immunization.

Special Groups

Three groups deserve special attention. First, all health care providers, especially if they come in contact with bodily fluids, should consider the three-part immunization against hepatitis B. Travelers should contact a local traveler's clinic or the health department at least two months in advance to learn what immunizations are required and recommended for their trip. Finally, those with HIV infection should be up-to-date with their immunizations, especially dT and pneumococcal and possibly measles and influenza. Avoid the OPV vaccine in these immunocompromised patients; the trivalent enhanced-potency, inactivated poliovirus vaccine (IPV) is recommended instead.

A new system was started last year for physicians to report adverse reactions to vaccines. Further information on the Vaccine Adverse Event Reporting System (VAERS) is available 24 hours a day at 1-800-822-7967.

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Intrauterine Devices and Pelvic Inflammatory Disease—A Reanalysis of the Literature

INTRAUTERINE devices (IUDs) are used less and less as a form of contraception in America. This is probably because of decreased marketing due to the litigation related to the Dalkon Shield. Additional concerns with IUDs include side effects of discomfort, increased bleeding, and the traditional belief that IUDs contribute to an increased incidence of pelvic inflammatory disease. There are two IUDs currently available in the United States. The Progestasert must be replaced every year and has a higher rate of ectopic pregnancy than other IUDs. The ParaGard (copper T 380A), a copper IUD, has a failure rate of about 3% and can be left in place for four years at a time.

All IUDs have an increased risk of pelvic inflammatory disease in the first 30 days. This is probably because of contamination of the uterine cavity during insertion. Other causes may include that the tail of the IUD allows bacteria to rise up the cervix and that the IUD will cause local inflammation in the area where it rests. For years, however, a belief has prevailed that IUD use leads to an increased risk of pelvic inflammatory disease after the first 30 days as well. This belief has recently been called into question. In cohort or prospective studies of women with IUDs, the risk of pelvic inflammatory disease was similar to that in sexually active women in industrial countries—about 1% to 2% in the 1970s. In a review of 17 case-control studies, it was found that these studies had often not corrected for oral contraceptive pill use in controls—that is, contraceptive pill use in controls may have provided protection from pelvic inflammatory disease. Those case-control studies that had 100% diagnostic accuracy (by using laparoscopy or laparotomy) and that corrected for oral contraceptive use show no or borderline statistical significance. In the remaining case-control studies after 1973, once there had been a great deal of publicity about the link between IUD use and pelvic inflammatory disease, both diagnostic bias (inflammatory disease being overdiagnosed in women presenting with abdominal pain who had an IUD in place) and referral bias may have skewed the data. Referral bias implies that the cases of pelvic inflammatory disease studied may not have been representative of all women with the disease. Women who had an IUD in place and had symptoms of pelvic inflammation were more likely to be referred by community physicians to a hospital. In the hospital, they were more likely to be included in studies than women in the community who had pelvic inflammatory disease but no IUD in place. Thus, women with pelvic inflammatory disease and an IUD in place may have been overrepresented in studies of risk factors leading to the disease.

This reevaluation of the data supports the position of a review of IUDs published in April 1989 in which the authors conclude that the IUD *can* be an acceptable method of contraception—especially for those women who are in the middle to older reproductive years, unable to take oral contraceptives, and in a stable, monogamous relationship and thus at low risk for sexually transmitted diseases.

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Physical Activity in Primary Prevention

IMPORTANT changes concerning exercise intervention were confirmed with the 1989 recommendations of the U.S. Preventive Services Task Force. The task force gave the same recommendation for counseling patients for physical inactivity as it gave for cigarette smoking and high blood pressure. Physical inactivity has long been recognized as a risk factor in coronary heart disease (CHD), but many physicians have felt to to be relatively unimportant compared with other risk factors such as cigarette smoking and elevated blood pressure. Recent studies have indicated that those who are not physically active have roughly the same risk of CHD developing as those with hypertension, hypercholesterolemia, or those who smoke. The strength of the association between physical inactivity and CHD is 1.9 compared with 2.1 for high systolic blood pressure, 2.4 for elevated serum cholesterol level, and 2.5 for smoking.

Researchers have found that physical fitness is associated with lower rates of all causes of mortality as well as CHD and cancer mortality. Further, the greatest reduction in relative risk occurred between the lowest level of fitness and the next lowest level. These data suggest that even modest improvement in fitness levels among the most unfit can result in substantial health benefits.

Counseling of physically inactive patients should emphasize regular, mild-to-moderate activity, such as brisk walking. More strenuous exercise activities should be deemphasized. In the past, exercise prescriptions typically suggested relatively intense activity, such as jogging, for 20 minutes at least three times per week. The task force now recommends that all patients should be counseled to engage in regular physical activity in a program tailored to their health status and life-style. Beginning exercisers should start with a regular, low to moderate level of exercise. Their goal should be to engage in an activity like brisk walking at least three times per week for at least 30 minutes.

Screening and intervention with physically inactive patients should specifically be included in periodic health examinations of all adults. A 1978 Harris survey found that most people reported they would be more likely to engage in health-promoting behavior if the recommendations came from their physician rather than from any other source. Inactive patients are most likely to comply with recommendations from their physicians for a regular pattern of exercise activity that can be maintained with minimal disruption of other aspects of their lives. Walking, when done briskly, is the ideal activity that meets these recommendations and can serve as a first step to more vigorous activities, if desired, in the future.

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Fifty Years of Psychopharmacology

An Interview with Benjamin Wiesel, M.D.

ALEX A. CARDONI, M.S.

EARLIER this year, Professor Alex Cardoni interviewed Dr. Benjamin Wiesel as part of the Oral History Program of the Hamilton Archives at Hartford Hospital. Dr. Wiesel is currently professor emeritus in the School of Medicine, University of Connecticut Health Center, and is in private psychiatric practice in Hartford. An abridged form of this interview is presented below. Readers who are interested in reading the complete interview should contact the Hamilton Archives.

Dr. Benjamin Wiesel was born and raised in New York City, obtained his undergraduate degree from New York University, his M.D. from New York Medical College, and completed psychiatry and neurology residencies at Bellevue and New York Psychiatric Institute. He served in World War II in Europe as a medical officer and psychiatrist and received the Bronze Star. In 1948 Dr. Wiesel came to Hartford as the first director of the department of psychiatry at Hartford Hospital, and held that position for 25 years. In 1973 he became head of the department of psychiatry at the University of Connecticut School of Medicine and held that position until 1977. He was instrumental in establishing the psychiatric partial hospitalization program at the Health Center.

Alex A. Cardoni is associate professor of clinical pharmacy at the University of Connecticut. He is also assistant clinical professor of psychiatry at the University of Connecticut School of Medicine and clinical pharmacology consultant for the department of psychiatry at Hartford Hospital. Since 1970 Professor Cardoni has worked in inpatient, outpatient, and partial hospital psychiatric services at Ohio State University, the University of Connecticut Health Center, and Hartford Hospital in conjunction with his teaching and research activities.

A.C.: What was life like 50 years ago for the practicing psychiatrist in terms of treating psychiatric patients with medicine?

B.W.: My interest and role in the field begins in the mid-1930s. So, when you talk about psychopharmacology and you start thinking of it in terms of the 1930s, you don't have very much to talk about because there were no such things as psychotropic drugs except those that had very brief actions like amphetamines, barbiturates, bromides, chloral, paraldehyde, and of course, the old standby, alcohol.

A.C.: Were any of these used more than the others?

B.W.: Amytal (amobarbital) mostly because the half-life of Amytal is so much longer than paraldehyde given rectally or orally. But Amytal would carry people (if you gave a high enough dose) and quiet them down through the night. That was the only real goal; there wasn't any concept at that time of changing a patient's thinking. Psychopharmacology was directed at brief behavioral control. Now, the picture is so radically different that it's almost impossible for younger people to visualize.

A.C.: Earlier you mentioned bromides. Were these used in treatment?

B.W.: In those days you used to find bromides easily available in drug stores, like Alka-Seltzer. You'd go in and there was a place that had tubes of tablets. You'd push your nickel in and push the lever and the tablet would drop down. If you'd feel nervous, you'd take your lunch hour from the office and throw in a couple of bromides. As a result we all became pretty expert in bromide psychosis. Bromide was common. You have a rash that goes over the bridge of the nose. You just take one look at the patient and you know it in a minute.

A.C. : When did reserpine come on the scene?

B.W.: Reserpine came temporarily in the early 1940s. It was derived from Indian *Rauwolfia*. I always thought it had something to do with the Hindu gurus who had such marvelous control that they could lie on a bed of spikes. When reserpine came out it was used as an antihyperten-

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ALEX A. CARDONI, M.S., Associate Professor, School of Pharmacy, University of Connecticut, Storrs.

sive drug and, I guess, was pretty successful. However, it created a problem because very clearly the effect of it was to induce depression. We saw many cases of depression due to reserpine. In fact, I never saw the extensive use of reserpine without it. It was marvelous to be able to make the diagnosis because it was one of the few ways of curing depression that we had—stop taking it! You felt like a miracle-worker.

A.C.: How long did you have to wait after stopping the drug before you started to see improvement?

B.W.: You'd have to wait a week.

A.C.: Did any new drug treatments come out of World War II as far as you can recall?

B.W.: None that I'm aware of. I guess there wasn't any pressure for it because nobody paid too much attention to shell-shock or combat fatigue cases except in the armed services.

A.C.: Let's talk about the 1950s. In 1954 the Smith, Kline, and French Company of Philadelphia marketed a drug called Thorazine. As they say, the rest is history. What was it like to be practicing during that time with this miracle drug now available to treat schizophrenia?

B.W.: There's no question about it, it was startling. It was the first time we had a drug which seemed to change mentation, thinking, which had all the characteristics of the medieval priest who could drive out delusions. One important factor was behavior control again. For example, with Librium, when you controlled DTs, you could treat alcoholics. When you could influence delusional thinking in schizophrenics with this new drug, you could treat them in a general hospital. So, the number of people who were in more severe degrees of illness were progressively taken into general hospitals as the drug scene changed therapeutically, starting with Thorazine. We now had a drug to cut down length-of-stay, enabling treatment in general hospitals and as outpatients. It was a whole new game.

A.C.: Was there wild enthusiasm to obtain and use the drug?

B.W.: Yes, there is no question but that it was grasped at.

A.C.: In 1954, when Thorazine was marketed, was it promoted as a cure for schizophrenia?

B.W.: I think that the expectations were that you treat these people for a long time and they recover. Some people had that expectation. And a lot of them did recover. But many didn't.

A.C.: How much written information came along with Thorazine? How much did you know about Thorazine before prescribing it?

B.W.: What was available back then was based upon studies done by people who were financed by the companies, so we looked upon them with some suspicion. But, it really was a matter of finding out for yourself. So most of us, I think, were pretty cautious. We took that information and applied it cautiously. I don't care how much all you people in the field say, "This is as safe as that; that's as safe as this." They're all unsafe; let's face it.

A.C.: Relatively unsafe.

B.W.: Relatively, but you have to do the best you can for the patient. I relieve my own anxiety by just not using them.

A.C.: The monograph for Thorazine in the 1955 *PDR* was 3/4 of one column of one page. If you look at the *PDR* in 1990, it's four pages, just for Thorazine.

B.W.: It takes a while to come out that you get bad rashes if your go out in the sun with Thorazine. You have to wait awhile before you get that information.

A.C.: We know that today, but back then...?

B.W.: It took a couple of years, I guess. That's true in the history of medicine with all drugs. I remember years ago, and probably very few people now living know anything about it, that Demerol was touted as an excellent substitute for morphine, but not addictive. Can you imagine what that was? It was the answer to a man's prayer. The result is that it was used a lot and it produced a lot of addiction. It took a couple of years before that got into the literature.

A.C.: Today there's great concern over the possible effects of tardive dyskinesia resulting from chronic use of antipsychotic drugs. Back in the 1950s, was tardive dyskinesia present, especially before these drugs made their appearance?

B.W.: No. Mostly we began to see it with large doses used in state hospitals. The very sickest ones got it. But, you know, with the patients being sent out with the changes in the system and the disgorging of patients from the state hospitals, they sent them out with a lot of medication. In some cases, patients were over medicated and we had tremendously successful results with these patients that we saw in clinics because we took them off of their medications! We had some absolutely amazing experiences. We'd take them off, the patient would get better. What got better? They were dopey, half-sedated, a little toxic. We took away the medication completely and gave them nothing. We'd say, "Just taper it off and come back in a month." They'd come back in a month and we'd say, "How do you feel?" They'd say, "Geez, I feel alive again." They might have been schizophrenic but were out of an episode. Most of them were people who just got repeated refills.

A.C.: What do you recall of the antidepressants that were marketed in the late 1950s and the antianxiety drugs in the early 1960s?

B.W.: Antidepressants are great drugs. I started a project with NIMH on lithium. I fell in love with the idea of lithium because it fit my needs—physiological illness and physiological treatment. I put all my private patients and everybody I could on lithium and watched them carefully. I thought it was great.

A.C.: That was later, though, wasn't it? That was in the 1970s.

B.W.: You could be right. I remember that it was approved only for the manic phase, but we were studying it for prevention of relapse. The results were great. I had some patients who got away with one episode or another per year. I found it very useful.

The antianxiety drugs are very, very helpful, but they do require control and understanding. There has to be some relationship between the patient and the doctor other than passing out a pill, because that leads to abuse and carelessness.

A.C.: In the 1940s we had the barbiturates; in the 1950s, we had meprobamate; 1960s, Librium; 1970s, Valium; 1980s, Xanax; 1990s?

B.W.: Every one of those has its abuse, notorious—Librium, Valium. 1990s? I don't know—Prozac?

A.C.: So far. I was thinking about the use of medication to control anxiety by that "decade" approach and it seems like, for each decade, there was one prominent medication used.

B.W.: We've got an answer and everybody agrees and look at the promotion. Madison Avenue gets on it and they start their promotion techniques. If they know that they've got something, they're going to put more ads and references on television. When you do that, you've got people's attention. They have to listen. Prozac? They don't have to do any advertising for Prozac; everybody's talking about Prozac. I walk into some place and its, "Say, what do you think about Prozac?" This was at my fish market. Everybody knows about Prozac. It helps the difficult cases of depression.

A.C.: What do you recall about meprobamate? Its a drug we don't hear about too much anymore.

B.W.: I believe that I read somewhere that there was an FDA or an NIH report on meprobamate—known as Equanil or Miltown—I don't know how many years back. The conclusion was that it was not dangerous, but also that it didn't do anything. That was my impression—that it didn't do anything. That didn't stop me from using it.

A.C.: I suspect that report came out early in the life of meprobamate because, by the late 1950s, there was enough clinical experience with the drug to show that it was highly addicting, did relieve anxiety generally, was toxic on overdose, and was not the safe alternative to the barbiturates that everybody thought it would be. Then, enter Librium to rescue people from this horrible drug meprobamate.

B.W.: You swap one for the other.

A.C.: What are your recollections of the MAO inhibitors, especially the early ones?

B.W.: The interesting thing to me is the historical part of it. There was a large tuberculosis ward at the U.S. Public Health Service Hospital on Staten Island where they made the observation about iproniazid (Marsilid) which was being evaluated for the treatment of TB. The Marsilid seemed to be making the patients a little lively, even slap-happy. I guess this was pretty obvious because you don't imagine that a TB ward is going to have too many people pretty cheerful. Their TB wasn't any different by X-ray. That's how they verified that observation and they started using it as an antidepressant.

A.C.: Did you use the early MAO inhibitors?

B.W.: Oh, yes. I used Marsilid right off the bat. That was the first drug. ECT (electroconvulsive therapy) is the first treatment for what I call the Lazarus syndrome. When I heard about Marsilid, that was it.

A.C.: This was the first antidepressant drug, even preceding the tricyclics. So the first antidepressant drug was an MAO inhibitor.

B.W.: Right. Unfortunately, what happened was that within two years they reported the first deaths with Marsilid—hepatotoxicity. I think I stopped it then. I think I was always a little bit leery, so I was pleased when the tricyclics came. But MAOIs are coming back. They dropped out for a long time because of liver damage. Apparently everybody feels pretty safe about it now, even the dietary people.

A.C.: On that note, we'll stop. I want to thank you very much.

B.W.: Thanks very much. It was fun.

The authors would like to thank Mr. Stephen Lytle, Archivist, Medical Library, Hartford Hospital, for his assistance in recording the interview.

Pediatrician's Response to a Stillbirth or Death of a Neonate

MORRIS A. WESSEL, M.D.

ON rare occasions, a nurse phones with the information that a mother who has chosen me to be her pediatrician has delivered a stillborn baby or has a newborn who has died in the first few hours of life.

A previous relationship with this mother often facilitates my being helpful at this sad moment. I may have met the expectant couple during a prenatal pediatric conference, or I may care for other children in the family. Frequently, parents I knew as children seek my pediatric services, so the relationship is long-standing.

As I leave my office or home to meet the grief-stricken parents at the hospital, I consider the difficult task they face as they cope with this tragic loss for which they had no preparation. A pregnant woman anticipates delivering a healthy baby and caring for her infant as the infant grows and matures. A man looks forward to seeing his wife holding their baby. He too anticipates cuddling and caring for his infant. He looks forward to the time the when he can take a toddler or preschool child for walks to the park or rides on the back of a bicycle. All of these precious dreams and hopes must be abandoned. The father, in addition to coping with his feelings of loss, also has the heavy burden of comforting the bereaved mother.

As I approach the hospital, I wonder how I can be most helpful to this couple. After four decades in pediatric practice, I am convinced that no relative, friend, or professional can reduce the anguish and grief associated with a significant loss but, by one's presence and concern, one can sustain and comfort bereaved individuals as they struggle with their loss.

I remember well a young woman, for whom I cared as an infant, child, and adolescent, who recently delivered a normal infant. She reminisced about giving birth to a stillborn infant the previous year. "People try so hard to bring you out of it," she said, recalling her anguish and grief. "That's no help...You can't escape your feelings when you have a stillborn. The nurses were great. They hugged me and sat with me, saying nothing. It was my friends who were impossible. One said, 'You're young. You'll get over it. Get pregnant again.' They meant well, but that wasn't the issue. I lost my baby and I needed to deal with it in my own way."

I remember well another mother who delivered triplets. Two were healthy and vigorous; the third was tiny and frail and died shortly after birth. I commented, "...you have two healthy babies." "Dr. Wessel," she said angrily, "that doesn't take away what I feel about losing the third one. I carried him for nine months. He was very much a part of me."

I have never made that mistake again! I know now that, at a time of a tragic loss, one's presence and concern (although appreciated) can only be supportive as individuals cope with their desolation.

There are ways of helping parents to begin the important process of grieving and mourning. An opportunity should be provided for parents, and grandparents also, to view and hold the baby. Many parents initially prefer to avoid this procedure. However, I believe it is important to suggest several times that parents take this opportunity, although one should not insist if they continue to reject the offer. Parents who do not take this opportunity often comment at a later date that they wish they had done so. Ten years after giving birth to a stillborn infant, a mother said to me, "I couldn't really mourn right. If I had only had a few minutes to cuddle and hold my baby, even though I knew she wasn't alive, it would have been easier."

It is important for physicians or nurses to offer help in arranging funeral plans. A brief service on the ward or in the hospital chapel, or elsewhere, is a way of saying goodbye, and it helps to initiate the mourning process. Many thoughtful nurses and social workers photograph the baby and offer these photos to the parents. If they choose not to accept the offer, the pictures are filed carefully. The need to have a picture to look at in the future is present, even if it is unrecognized at this moment in most individuals. Parents frequently contact hospital personnel weeks, months, and often years later to request these pictures.

MORRIS A. WESSEL, M.D., Clinical Professor Pediatrics, Yale University School of Medicine, New Haven.

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Grieving and mourning is a painful, exhausting task. Women who have lost a baby often experience feelings of weakness, bodily loss, and numbness. Their bodies often ache, particularly their arms—the arms in which they had anticipated cuddling a baby. Men, too, have intense feelings of loss. They also struggle to console their wives, a task which is heartrending and difficult. Only time can diminish the intensity of these feelings.

Doctors, nurses, and friends are familiar with the utter helplessness one feels when faced with grieving parents. We can be sustaining by our presence, our interest, and by initiating frequent contacts during this period. Attending a funeral service, sending a brief note of sympathy, or visiting the family at home demonstrates one's concern during this difficult time.

When there are other children in a family, one has the additional responsibility of helping them during this difficult time. Children are often at a loss to understand why their mother failed to return home with a new baby as promised and why both parents seem so strange. One needs to explain in simple terms: "The baby was too small and too weak to live. He (or she) died."

Three-year-old children, some even younger, can grasp the concept of death by being told simply that "the baby is no longer living" or that "he (or she) is just resting without feeling or breathing." A child who has experienced the death of an animal, such as a bird, pet dog, or cat, can grasp the idea of the permanence of death a bit more easily than if he or she has never had this previous experience with death.

Parents are likely to be so preoccupied with their own grieving that their children may feel abandoned as they struggle alone with their own feelings of sadness. One should advise parents to explain to their toddlers and preschool or older children: "Mommy and daddy are very sad because the baby didn't live." This explanation, even to a very young child, can be helpful, for it encourages a child to be sad also.

A physician, nurse, or social worker who maintains an ongoing relationship with families during bereavement demonstrates to parents and children that someone cares about them. This task is time-consuming and exhausting, but I find this role to be one of the most satisfying aspects of being a primary physician. "To cure sometimes, to relieve often, to comfort always" is as an important a guideline today as when Edward Trudeau popularized this conceptualization in the early part of this century.

Suggested Reading

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Hispanic Health in the United States

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Hispanics are the fastest growing minority in the United States. Typically, they are divided into five subgroups: Mexican American, Puerto Rican, Cuban American, Central or South American, and "other" Hispanics. Risk factors for morbidity and mortality vary among these subgroups. Use of health care services is affected by perceived health care needs, insurance status, income, culture, and language. Compared with whites, Hispanics are more likely to live in poverty, be unemployed or underemployed, and have little education and no private insurance. Hispanics are at an increased risk for certain medical conditions, including diabetes, hypertension, tuberculosis, human immunodeficiency virus infection, alcoholism, cirrhosis, specific cancers, and violent deaths. Proportionate to their representation in the population, there are few Hispanic health providers, emphasizing the need for all medical personnel to be knowledgeable about Hispanic health care needs.

POVERTY, lack of education, and access barriers to health care predispose many American minorities to disproportionate mortality and morbidity. Hispanics are the fastest growing minority in the United States. Since 1980, the Hispanic population has increased 34%, while the non-Hispanic population has increased only 7%. In March 1988, there were 19.4 million Hispanics in the United States.[1,2] By 2000, Hispanics will number an estimated 31 million, the largest minority group in the United States.[3]

Certain factors contributing to morbidity and mortality features are endemic among Hispanics, particularly when examined by subgroup. In addition, cultural norms, poor knowledge of English, and socioeconomic status affect Hispanics' use of health care. Compared with non-Hispanics, Hispanic families are more then 2½ times as likely to live below the poverty level.[1] Poverty and lack of health insurance contribute to the Hispanic health care challenge of today. This report examines these concerns and suggests ways for the American Medical Association to educate physicians about the health needs of this growing population.

Background

Demographics

The Hispanic population has diverse national origins and cultures. The literature divides Hispanics into five subgroups: Mexican American, Puerto Rican, Cuban American, Central or South American, and "other" Hispanics.

Persons of Hispanic descent may have recently moved to the United States or their families may have lived here for centuries. Hispanics may be bilingual, speak only English, speak only Spanish, or speak a little of both. When Spanish is spoken, Hispanics often use different idioms among subgroups, which makes communication confusing among the different groups. In addition, cultural values, education, and family income vary by subgroup. Most of the literature focuses on Mexican American, Puerto Ricans, and Cubans. Scant data exist on Central or South Americans and other Hispanic subgroups.

From the Council on Scientific Affairs, American Medical Association, Chicago, Ill.

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all the facts and circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and patterns of practice evolve. These reports reflect the views of scientific literature as of August 1990.

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States With the Largest Hispanic Populations, 1988*

State	State's Hispanic Population, in Thousands	State's Total Population of Hispanics, %	State's Hispanic Population as Share of US Hispanic Population, %
California	6762	24.3	33.7
Texas	4313	25.8	21.5
New York	1982	11.2	9.9
Florida	1586	12.7	7.9
Illinois	855	7.5	4.3
Arizona	725	20.8	3.6
New Jersey	638	8.4	3.2
New Mexico	549	36.7	2.7
Colorado	421	13.0	2.1

*Data from the US Bureau of the Census.[4]

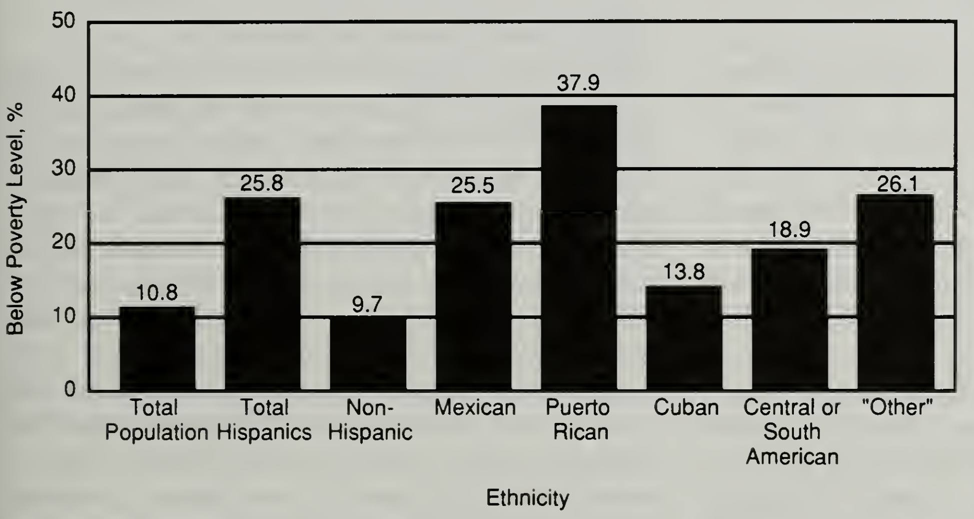

Fig 1.—Percent of families below the poverty level in 1987. Data from the US Bureau of the Census.[1]

Of the 19.4 million Hispanics in the United States, 62.3% are of Mexican origin, 12.7% are Puerto Rican, 5.3% are Cuban, 11.5% are Central or South American, and 8.1% are of other Hispanic origin. Subgroups tend to concentrate in different geographic areas, with Mexicans in California and Texas, Puerto Ricans in New York, and Cubans in Florida. Chicago has the most diverse cultural groupings, with proportions similar to the national divisions.[1,2] The Table further breaks down the Hispanic population by state.[4]

High birthrates and immigration account for the rapid Hispanic population growth in the United States. Compared with the fertility rate of the general population (65 of 100 births), Hispanics have a higher fertility rate (97 of 1,000 births), give birth to children at younger ages, and have more children.[3] Since the median age of Hispanics is 25 years and males and females are proportionally distributed, the high birthrate is expected to continue.

As of 1988, about half of all Hispanics completed 12 years of schooling. However, more than twice as many non-Hispanics as Hispanics finished four or more years of college. Less education predisposes Hispanics to high unemployment rates and poverty. Lack of education may also limit Hispanic understanding and use of the U.S. health system.

Employment rates differ slightly between Hispanics and non-Hispanics, but proportionally many more Hispanics (8.5%) are unemployed compared with non-Hispanics (5.8%). For Hispanics, the 1988 mean income was $25,736, in contrast to $37,388 for non-Hispanics. Compared with non-Hispanics, Hispanics are more then 2 ½ times as likely to live below the poverty level. Of the subgroups, Cuban Americans have the highest incomes, while Puerto Ricans have the lowest. Nearly 40% of Puerto Ricans live below the poverty level, in contrast to about 14% of Cubans (Fig 1).[1]

Despite their lower incomes, Hispanics spend proportionally more of their disposable income on health care. Yet as a group, Hispanics are more likely than the general population to be uninsured. Cuban Americans, with the most education and highest incomes, are the most likely to have private health insurance (74%). Puerto Ricans, with the lowest incomes and highest unemployment rates, are most likely to have Medicaid coverage (32%). Although more Mexican Americans than Puerto Ricans are employed, they are the most likely to be uninsured (30%) (Fig 2).[5,6] Mexican Americans who work tend to have jobs with no insurance benefits and/or they cannot afford insurance premiums for their large families.[4]

Use of Health Care

Use of health care by Hispanics is affected by perceived health care needs, insurance status, income, culture, language, and other factors that are beyond the scope of this report. Based on data from the National Health Interview Survey, Mexican Americans, who have the least insurance, visit physicians least often. Puerto Ricans have the highest physician visit rates, suggesting that persons on Medicaid have greater access to care than other poor, uninsured groups and that they tend to have more severe illnesses than those who are employed and insured.[6,7]

Preliminary data from the Hispanic Health and Nutrition Examination Survey (HHANES) of the National Center for Health Statistics, conducted in 1982 to 1984, confirm these trends. Compared with whites, about half as many Hispanics have a regular source of health care.[8] Thirty-nine percent of Puerto Ricans had a physical examination within a year, compared with 34% for Cubans and 25% for Mexican Americans.[3] Excluding Cubans, only about 60% of Hispanics initiate prenatal care in the first trimester, compared with 80% of whites. Hispanics are three times as likely as non-Hispanics to receive no prenatal care. Among the subgroups, Puerto Ricans received prenatal care later and less often.[3] Variation in Medicaid coverage may exist because of concentrations of Hispanics of different national subgroups in states with high Medicaid eligibility requirements.

Compared with whites, twice as many Hispanics report using the emergency department as a source of primary care. Digestive disorders and physical impairment constitute the most frequent presenting problems vs other potentially more serious conditions, such as circulatory and respiratory difficulties.[9] In addition, Hispanics are more apt to enter hospitals via emergency departments. Compared with whites, Hispanics have longer and more expensive hospital stays.[10]

Health care use is also governed by access to comprehensive and preventive health care. Overall, Hispanics are less likely to have private insurance than either whites or blacks.[11] Working Hispanics are more likely to be underemployed, employed part-time, or have jobs with no insurance benefits. Jobs that do offer insurance may impose high copayments for employees, which Hispanics often cannot afford to pay because of large families. This lack of insurance restricts Hispanic access to adequate health care.[11,12] As an urban and poor minority, Hispanics receive the most health care from large, public hospitals that have rotating staffs, particularly for patients on Medicaid or other public funding.[13] In such settings, patients rarely experience continuity of health care. Hispanics who have no insurance or have public funding find themselves seeking care from institutions that focus on tertiary rather than primary care.

Low incomes and lack of health insurance restrict Hispanic access to primary health care more than any other variables.[11] Expanding Medicaid coverage to include everyone below the federal poverty level and mandating that employers offer health insurance for reasonable premiums would help Hispanics who have little or no insurance coverage.

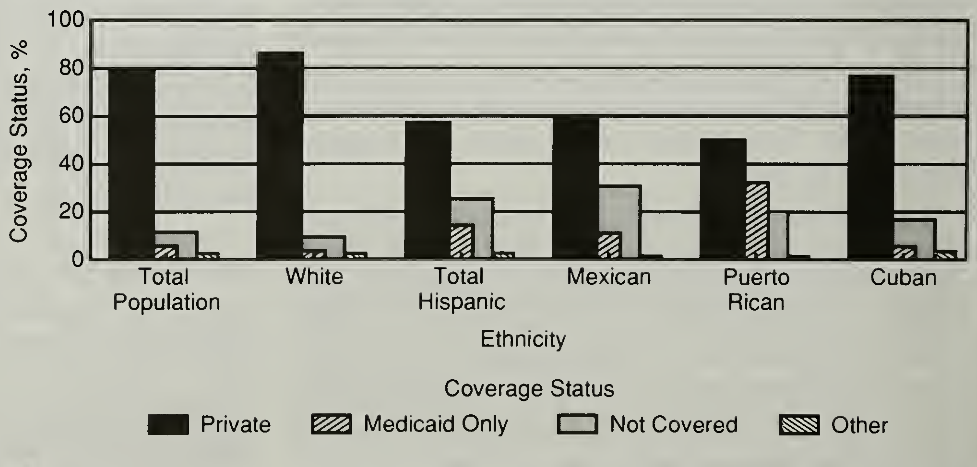

Fig 2.—Insurance status of persons younger than 65 years in the Standard Metropolitan Statistical Area in 1978 and 1980. Data from Trevino and Moss.[6]

In addition, Hispanics face cultural and language barriers. Although Hispanics constitute 7.9% of the U.S. population, less then 5% of all U.S. physicians and students in medical school are Hispanic.[14] Differences in culture and language from that of most health care workers contribute to a lack of use of preventive care by Hispanics. For example, Hispanic patients who speak English are more likely to have a regular source of medical care compared with those who speak only Spanish.[15] Because Hispanics, blacks, and other minorities are underrepresented in medical schools, the American Medical Association has encouraged the recruitment and retention of these students.[16,17]

Furthermore, patients who are poor and do not speak English well or at all and who feel estranged from the complicated U.S. health-care system encounter complex obstacles to accessing preventive care. Acculturation, or the adaptation of persons from one culture to another, influences Hispanic use of health care. A recent study of Mexican Americans showed that less acculturated persons had significantly lower likelihoods of outpatient care for physical or emotional problems. Even when controlling for need, the less acculturated patients with Medicaid used inpatient services four times less than the more acculturated patients with Medicaid.[18] Other research supports the hypothesis that Hispanics need services but are reluctant to use them because of barriers related to culture and language. When researchers manipulated variables by minimizing cultural and language obstacles, Hispanic use of the health services at that facility increased.[19]

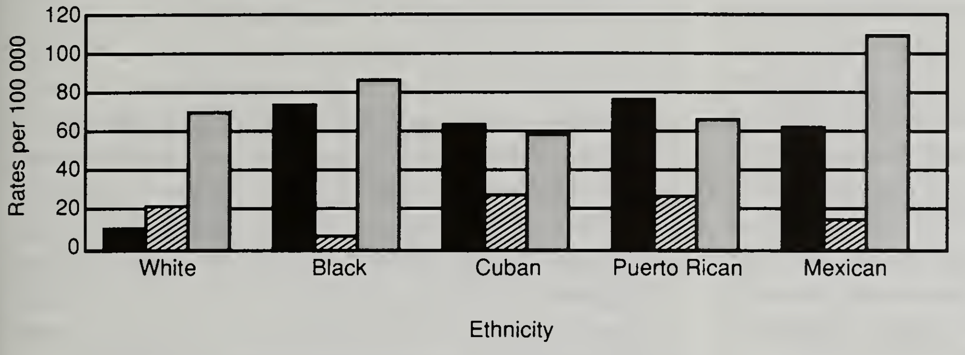

Fig 3.—Male age-adjusted homicide, suicide, and accident death rates in the United States from 1979 to 1981. Solid bars indicate death by homicide; hatched bars, suicide; and dotted bars, accidents. Data from Rosenwaike.[25]

At times, Hispanic patients may be more likely to perceive their illnesses according to folk practices. Folk-defined illnesses or culture-bound syndromes have intrigued researchers over the years, and as a result they may be more of an artifact in the literature than a prevalent cultural influence. Hispanic patients may describe their illnesses according to their cultural understanding. For example, patients may complain of a fright sickness known as *susto* or a fighting attack called *ataque*. Often these complaints have biologic bases that need careful and sensitive medical exploration to accurately diagnose and treat the illness.[20-22]

Controversy exists among Hispanic health experts concerning the frequency with which folk healers, or *curanderos*, are used. Anderson et al[23] note that while up to 20% of Hispanics may regularly use home remedies, the use of folk healers may be infrequent. Pedro Poma, M.D., believes this practice varies considerably among the cultural subgroups and that the practice is fairly widespread in some subsets (oral communication, April 1990).

When communicating with a Hispanic patient, health care providers are often, either directly or indirectly, communicating with the patient's family. Most Hispanic families emphasize interdependence, affiliation, and cooperation. Important decisions are made by entire families, not individuals.[3] Thus, Hispanic patients may discuss the physician's diagnosis and treatment recommendations with their families before deciding to follow them.

Hispanic Health Status

Mortality

Accurate estimates of Hispanic death rates are impossible to determine because, until 1988, the national model death certificates did not contain Hispanic identifiers.[3] Although some states incorporated Hispanic origin on their death certificates, such reporting is not uniform and lacks precision. For example, funeral directors completing death certificates may indicate ethnic origin by observation rather than by inquiry with family.[24] The standardized collection of consistent vital statistics on Hispanics by designated state agencies would provide more accurate data.

Nevertheless, researchers have attempted to study Hispanic mortality rates by examining surnames on death certificates and by reviewing 1979 to 1981 mortality data tapes from the National Center for Health Statistics, which classified deaths by age, sex, cause of death, and place of birth.[3,25,26] Overall, Hispanics die of the major national killers: heart disease, cancer, and stroke.[3] Compared with the general population, Hispanics suffer from excess incidence of cancer of the stomach, esophagus, pancreas, and cervix.[27] Death due to stomach cancer is twice as high for Hispanics as for whites.[3,27,28] Hispanic women suffer from cervical cancer twice as often as white women,[3,27,29] but their five-year survival rates slightly exceed those of whites.[30]

Alcoholism and cirrhosis are prevalent among Hispanics, particularly Mexican Americans and Puerto Ricans.[3,31,32] Mexican-born men have a 40% higher risk of death due to cirrhosis then white men. A review of autopsies from the University of Southern California Medical Center between 1918 and 1970 revealed that 52% of all deaths of Mexican-American men aged 30 to 60 years were due to alcoholism, compared with 24% for white men.[31] In addition to alcoholism, Hispanics share a disproportionate number of deaths due to narcotic addictions.[3]

Violent deaths account for high mortality rates among male adolescents and young adults of Mexican-American, Puerto Rican, and Cuban origin.[25,26] All three Hispanic male subgroups exceed white male deaths due to homicide. Puerto Rican males have higher death rates due to homicide than black males. Cuban and Puerto Rican males surpass white males for suicides. Accidents occur most frequently among Mexican-American males and least often among Cubans (Fig 3).[25]

Morbidity

Of the three major subgroups, Puerto Ricans report the worst health status. In 1979 to 1980, more Puerto Ricans reported chronic health problems as a limitation of their major activities than blacks, Mexican Americans, and Cubans. At the same time, compared with whites and other Hispanic subgroups, Puerto Ricans had the highest incidence of acute medical conditions.[6,20]

Compared with whites, Hispanics have three times the risk of diabetes.[12,33] Obesity and diet are largely correlated with diabetes in Hispanics. The HHANES study revealed that 26.1% of Puerto Ricans, 23.9% of Mexican Americans, and 15.8% of Cubans aged 45 to 74 years have diabetes.[31] In addition, approximately 30% of males and 39% of females of Mexican-American descent are overweight, as are 29% of males and 34% of females of Cuban descent and 25% of males and 37% of females of Puerto Rican backgrounds.[34] Mexican-American women suffer from gallstones twice as frequently as white women. In addition, Mexican Americans have a higher incidence of gallbladder cancer than whites.[12,35]

Not only do more Mexican Americans have diabetes than whites, but their disease is also of greater metabolic severity and places them at higher risk for complications. For example, Mexican Americans suffer a higher prevalence of diabetic retinopathy. In addition, the incidence of diabetes-related end-stage renal disease has been reported to be six times that of whites.[35] Given the Mexican-American propensity for obesity and diabetes, it is not surprising that this group also tends to have higher levels of cholesterol and triglycerides than whites.[36,37] Despite these potential risks, the incidence of cardiovascular mortality is not greater for Mexican Americans than whites.[3,35,37]

In general, Hispanics who are poor exhibit a higher risk for unrecognized and untreated hypertension.[3,37-39] Also, hypertension is more prevalent among Hispanics than whites.[3,12,37] Data from the HHANES study indicated that almost half of the Puerto Ricans surveyed with hypertension did not know they had it.[40] Cigarette smoking among Hispanics contributes to their risk for cardiovascular disease. According to data from the HHANES study, 43.6% of adult Mexican-American men smoked compared with 41.8% of Cuban men, and 41.3% of Puerto Rican men.[41] A San Francisco (Calif) study revealed that men who are less acculturated have higher smoking rates and women who are more acculturated smoke more than their less culturally adapted counterparts.[42] Researchers link smoking with the nearly doubling of lung cancer rates among Hispanic men and women from 1970 to 1980.[31]

In addition to an increased risk for lung cancer, the incidence for tuberculosis is 4.3 times greater for Hispanics than whites.[43] From 1980 to 1987, New York City experienced a marked increase in tuberculosis cases, especially among 30- to 39-year-old Hispanics. Researchers suggest this increase relates to latent tuberculosis infection, which is activated by the human immunodeficiency virus (HIV) among Hispanics in that city.[43]

Although Hispanics constitute only 7.9% of the US population, they account for 14% of reported acquired immunodeficiency syndrome (AIDS) cases, nearly 21% of AIDS cases among women, and 22% of all pediatric AIDS cases.[3,44] Hispanics are at greater risk for HIV infection, not because of their race and culture, but because of underlying factors such as living in high-prevalence areas and exposure to intravenous drug use.[44] Most of the Hispanic AIDS cases in the Northeast are among intravenous drug users. Heterosexual transmission of HIV from intravenous drug users to their sexual partners is more prevalent among Hispanics because of cultural restrictions against the use of condoms[45] (Navarro M. AIDS and Hispanic people: a threat ignored. *The New York Times*. December 29, 1989: 1, 4). The 1987-1988 National Center for Health Statistics Survey indicates that Hispanics know less about HIV and AIDS than non-Hispanics.[46] An Oregon survey of Hispanic outpatients revealed that only 50% thought condoms could help prevent transmission of HIV.[47] Because certain groups are at risk for HIV infection through drug use and because cultural differences may affect the understanding of HIV transmission, the American Medical Association suggests that AIDS prevention education programs be tailored to subgroups (such as Mexican Americans and Puerto Ricans) considering their cultural and language differences.[48]

Perhaps related to cultural restrictions on the use of condoms and the cultural importance of motherhood and child rearing, Mexican-American females tend to have high rates of teenaged pregnancies and high-parity births. According to 1983 and 1984 data from 23 states, 31% of Mexican-American females and 30% of Puerto Rican females aged 15 to 19 years have given birth.[3] Despite the young ages at the time of pregnancy and the lack of prenatal care, Hispanic females, especially Mexican Americans, have lower rates of premature deliveries and low birth weight.[3,49,50] Among the subgroups, Puerto Ricans have the highest birthrates for unmarried young women and the highest infant mortality attributed to low birth weight. Puerto Rican poverty and its effect on access to health care contribute to this group's lack of prenatal care and concommitant infant mortality.[12,51] As Hispanic women become more acculturated, the risk of giving birth to low birth weight babies increases.[50] In addition, increased acculturation is associated with decreased breastfeeding of infants. These trends, combined with the fact that Hispanics are three times more likely than non-Hispanics to receive *no* prenatal care, contribute to the morbidity of urban, poor Hispanic mothers and infants.[3]

Summary

Hispanics are the fastest growing minority in the United States. As a heterogeneous group, Hispanics are multicultural and can be monolingual or bilingual. They are divided into five subgroups: Mexican American, Puerto Rican, Cuban, Central and South American, and other Hispanics. Poverty, little education, lack of insurance, and high unemployment rates pose barriers to health care for Hispanics.

Poverty and lack of health insurance are the greatest impediments to health care for Hispanics. Use of health care services by Hispanics is affected by perceived health needs, socioeconomic status, insurance, language, and culture. Many Hispanics who work cannot afford insurance premiums. Those without insurance who report health needs avoid the health system until they are ill. The literature suggests that as Hispanics adjust to the U.S. health system, both culturally and linguistically, they will use health services more often and more beneficially.

The literature also suggests that as Hispanics become more acculturated, their health status worsens. Hispanics increase their use of tobacco and consume a less healthy diet as they adapt to the U.S. culture. As Hispanics live longer in the United States, their morbidity and mortality rates for certain diseases increase. Hispanics suffer a disproportionate share of AIDS cases, and males are more likely to die of violence. Diabetes, hypertension, tuberculosis, certain cancers, and alcoholism rates are higher for Hispanics than for whites.

By working with Hispanic health organizations on health promotion and disease prevention through community advertisement and education and by increased recruitment and retention of Hispanic medical students, the medical system can help Hispanics become more involved with their own health care. In addition, Spanish-language preventive health literature can help the less acculturated understand and use the health system appropriately. Finally, medical research geared toward decreasing the disproportionate rates of mortality and morbidity among Hispanics will contribute to the greater well-being of all Hispanics and to the knowledge and skill of all health providers.

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The Needle

E. TREMAIN BRADLEY, M.D.

I am about to give my patient the needle. No, my intention is not to vex him with gibes. Well, it might mean I will try goading him into doing what I feel is best for him. But usually it indicates that he is about to be attacked with a long, hollow, slender piece of metal with a sharp bevel on the end. He may experience pain from any of these, and would prefer to avoid it. How?

In the first instance, the psychological pain can be avoided by not teasing and barbing to the point of vexation. In the second instance, logical persuasion with sympathetic outlining of facts and probabilities is kinder and often more effective in helping one to make the right decision. But thirdly, that nasty needle! It hurts! Or does it have to?

What is the purpose of piercing the skin? Intradermal injections, as for testing sensitivities, are going to sting no matter what, since the fluid introduced pulls the skin cells apart and away from the sensory nerve endings.

But what happens when fluid is to be introduced below the skin? First, the needle must pierce the skin. Again painful? Not necessarily. Most important is using a sudden—staccato—thrust vertically through the skin. Some people successfully slap the skin just before the jab, as a counterirritant or distraction. I prefer to squeeze lightly a bunch of tissue at the site of election, in a series of rapid squeezes, almost like a tremor, ending with a firmer squeeze, followed immediately, almost simultaneously, by the dart-like puncture.

Once the needle is in and at the depth desired, any medication to be given is slowly expelled from the syringe while a gradual massage is administered by the "squeezing" fingers. Withdrawing the needle, of course, is no problem.

But suppose the object is to produce local anesthesia. A small gage needle may be used to start with, placing a little of the agent just near the point of entry. To numb a large area I like a long #22 needle introduced at the same spot, now painless. It can be run far along in the loose subcutaneous tissue usually with no pain if the point is kept away from, yet close to, the undersurface of the skin, and away from the underlying structures. The anesthetic agent is then introduced slowly *only* as the needle is being withdrawn. The same procedure can then be followed in one or many other directions.

My wonderful and long-suffering (28 years with me) nurse, Gladys Dowling, and I competed, taking pride when the patient was unaware that the injection had been given. Nothing the matter with a little fun in your practice, especially when it benefits your patients!

E. TREMAIN BRADLEY, M.D., solo practice of general surgery, retired to Norfolk, CT.

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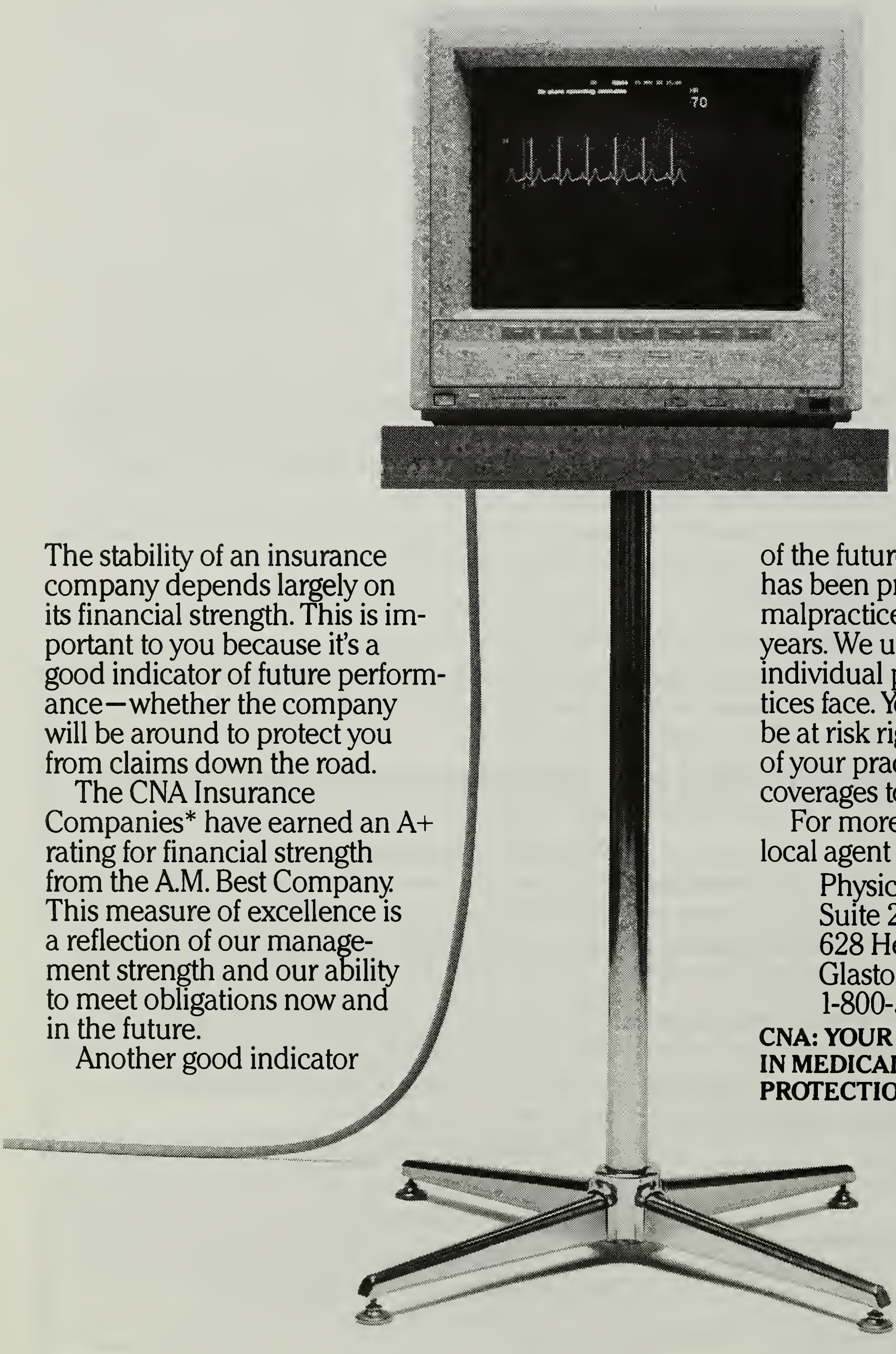

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Guest Editorial

Luck and the President's Health

George Bush was lucky. That seemed to be the general reaction when President Bush's recent heart and thyroid problems were quickly diagnosed and treated. Within hours, we learned he had suffered atrial fibrillation, a fluttering of the upper chambers of the heart. His doctors reported a few days later that his heart's uneven pumping was caused by an overactive thyroid, linked to Graves' disease. Mr. Bush received medications for his heart and is now on drugs for his thyroid. Although the story has developed new angles—first dog Millie's lupus and Barbara Bush's own thyroid problem have raised questions about possible environmental causes and their relationship to autoimmune diseases—it must still be remembered that the president received quick and appropriate care when he needed it.

On the surface, the handling of Mr. Bush's illness was a perfect example of modern medicine at work, so perfect that it seemed routine. Physicians recognized the problems, knew what to do and did it. But under the surface, to those of us who are aware of the research that underpins medical practice, it was one more demonstration of how top-notch care—not only for those in high office but for all of us—depends so much on scientific discoveries.

Imagine a world without such discoveries, without the know-how to unearth facts where they lie. The ancient Greeks, admirable for so many things but preferring speculation to direct observation and experimentation, lived in such a world. They did not know that the heart pumped blood; they surmised that blood just swished back and forth in the body. They believed that arteries carried air (the Greek-based word, "artery," means air-carrier). They thought that the brain was an air conditioning unit for the blood. It took reawakened interest in the natural sciences during the Renaissance, and the relentless quest for knowledge that has gone on ever since, to create today's medicine.

It is no exaggeration to say that the medical personnel taking care of President Bush's atrial fibrillation owed a great deal to the basic research done on the body's circulation by the English physician, William Harvey, back in the 1620s. Harvey discovered how circulation works in the body (he compressed veins to determine blood flow, much like learning the direction of a very slowly moving stream by damming it up to see which side pools up). Harvey also figured out the functions of the heart's four chambers. Discoveries since then in the field of cardiology—there have been many, and there will be more—all derive from Harvey's work.

As for the president's thyroid problem, credit for understanding the gland's functions and malfunctions has to go partly to a German biochemist and a Cleveland physician. The biochemist, Baumann, discovered in 1896 that the thyroid gland, located just below the Adam's apple, contained iodine while all other tissues had practically none. In itself, this finding meant little at the time. It was simply a curious piece of added information about the human body, just like the many pieces that are added every day, year by year.

As often happens in science, it did mean something to someone else eventually—to the Cleveland physician, David Marine, 10 years later. Noticing that an unusual number of his patients had goiter, a disease marked by a sometimes disfiguring enlargement of the thyroid, Marine began to wonder if the iodine-hungry gland might be reacting to an iodine deficiency. His subsequent treatment of goiter patients with iodine compounds worked and was generally accepted by the mid-1920s. Marine then thought: Why not put iodine in drinking water supplies or in table salt so everyone would benefit routinely? That idea was also accepted, and that is why today we have iodized salt, and simple goiter is almost nonexistent.

So, obviously, there was more than good luck favoring President Bush. His doctors had the benefit not only of their modern training but of decades of basic biomedical research to guide them in understanding the president's atrial fibrillation first of all, and then his thyroid problem.

Now here is a question to ponder: Will whoever is president in the year 2091 benefit from scientific findings yet to be made? Or, on a more personal level, will your grandchild's grandchild? Will cancer be conquered by then? Heart disease? Diabetes? Stroke? AIDS? Arthritis? Alzheimer's? Some of the answers rest with scientists working right now in basic research laboratories all over the globe, quite possibly here in Connecticut. Much of their work is arcane, much of it subtle, nearly all of it done out of the limelight. Their successes, though they may reverberate throughout the scientific world and lead to Nobel Prizes, are unlikely to rate a 60-second house call on TV.

Because basic research takes place behind the scenes

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and beyond the average person's understanding, the need to keep it a top priority tends to be forgotten. Unfortunately, this seems especially so at the dawning of this decade. This year, the nation's health-care bill will rise to a projected 13.7% of the gross national product. That represents a whopping $756 billion, a sum definitely worth trimming. Yet, while NASA got more than $12 billion last year, the National Institutes of Health (the prime funding source for basic research) received less than $8 billion. While only 24% of research grant requests now get approved and funded by NIH (compared with 33.6% in 1980), the cost of one Stealth bomber could fund 6,000 grants.

It is ironic, because basic biomedical research saves money in the long run. The polio vaccine and fluoridation, important advances that came out of research laboratories, have substantially reduced polio and the incidence of tooth decay. They have also resulted in huge savings in the nation's health care bill. One study has shown that for every dollar invested in medical research between 1975 and 1990, the return on investment to the economy has been $13 in reduced health care costs, absenteeism, productivity loss and other consequences of disease.

Discoveries coming from basic biomedical research hold the most promise for reducing the three M's—money, mortality and morbidity. By those, I mean the high cost of health care, the deaths that might be avoided, and the lowered quality of life brought on by disease.

According to public opinion polls, Americans know that too little is invested in medical research. The need, therefore, is to convince state and federal decision makers. They must be made aware, as they wrestle with the cost of health care, that an essential part of the solution is to control diseases in the first place. That can only come by understanding the causes of diseases, which in turn comes about from the conduct of basic research. We should ensure that the vitality of the national's biomedical research enterprise is not further eroded. Indeed, it should be reinvigorated.

Can we Americans afford to support basic research? We spend more than $1 billion a year on popcorn and over $700 million on peanuts—and $500 million on research on our No. 1 killer, heart disease. We spend $5 billion a year at movie theaters and $1.7 billion on Nintendo games—and $1.5 billion on cancer research. Can we afford to support basic research? We cannot afford not to. The president—and we—should never have to depend on dumb luck.

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Peter M. Zeman, M.D., *Director*
Impaired Physicians Program

Richard M. Bridburg, M.D., *Director*
Consultation Services

1991 Legislative Results

Never has medicine in this state been under more serious attack than during the 1991 regular session of the Connecticut General Assembly. We faced attempts by seniors for mandatory Medicare assignment without income limits, allied medical professions determined to extend the scope of their practices without benefit of medical training or licensure, and legislative initiatives to replace the medical licensing board with " independent" lay hearing panels for physician discipline.

It was a most difficult and strenuous time for our CSMS legislative staff and lobbyists, but thanks to their diligence and to the good will of the many legislators involved, and most of all, thanks to the timely outpouring of testimony, letters, telegrams and phone calls from so many of *you*, my colleagues, medicine's professionalism has emerged intact, and perhaps even strengthened. Indeed, there is *no* substitute for *your* CSMS membership, *your* professional solidarity, and *your* prompt, personal action. Congratulations!

Disciplinary Hearings: A revised bill on physician discipline (**P.A. 91-105**) has been signed by the governor. The new legislation includes:

— The Medical Examining Board retains its current composition but no member can serve for more than eight years.

— The governor retains the authority to nominate members; however, all candidates must be approved by the General Assembly.

— Public members cannot have immediate family members who are physicians.

— The Department of Health Services must file charges with the Board within 60 days if a physician is a threat to patients.

— Sub-panels of the Board will be appointed to conduct hearings and all subpanel members must be present at hearings. Each panel member will be allowed one excused absence per hearing if necessary.

— The full Board must then act within 90 days of the subpanel's recommendation and must decide to suspend or revoke a license. (Time period can be extended for good cause).

Mandatory Assignment: H.B. 7010 would have required physicians to accept Medicare assignment with no income limits; it was voted on favorably by the Human Services Committee, referred to the Appropriations Committee and died there 31-11.

Utilization Review: **S.B. 844,** which licenses and regulates private utilization review companies, passed the House and Senate and awaits the governor's signature.

Mandated Free Care: **S.A. 91-9** is a study bill, to explore the possibility of all health care providers donating their services one day per month to the uninsured. Amended to remove a section to study conditioning licensure on free care, it was voted out of the Senate and the House, and signed by the governor. We have submitted the names of Roger Beck, M.D., and Joseph Czarsty, M.D., to serve as CSMS representatives on this study committee.

Other Bills: **P.A. 91-168** requires practitioners who recommend a diagnostic test, to reasonably inform the patient of the test's approximate range of costs. An amendment was added to require those with a financial interest in the diagnostic imaging equipment to disclose it to the patient beforehand. It has been signed by the governor.

H.B. 7339 makes comprehensive changes to the Workers' Compensation System, allowing employers to set up a "preferred provider" system. However, employees may go outside the system, but those physicians outside the system would only be paid the "preferred provider" rate.

P.A. 91-283 amends the present living will statute to reflect recent court decisions on evidence of a patient's wish not to allow extraordinary measures in the final stages of life, including withdrawal of artificial nutrition and hydration.

BILLS THAT DIED: **H.B. 5111** would have allowed physical therapists direct access to patients. The bill died 15-7 in committee.

H.B. 6115 would have required HIV-positive health care providers to disclose their status to patients. The bill was never put on the agenda for a vote.

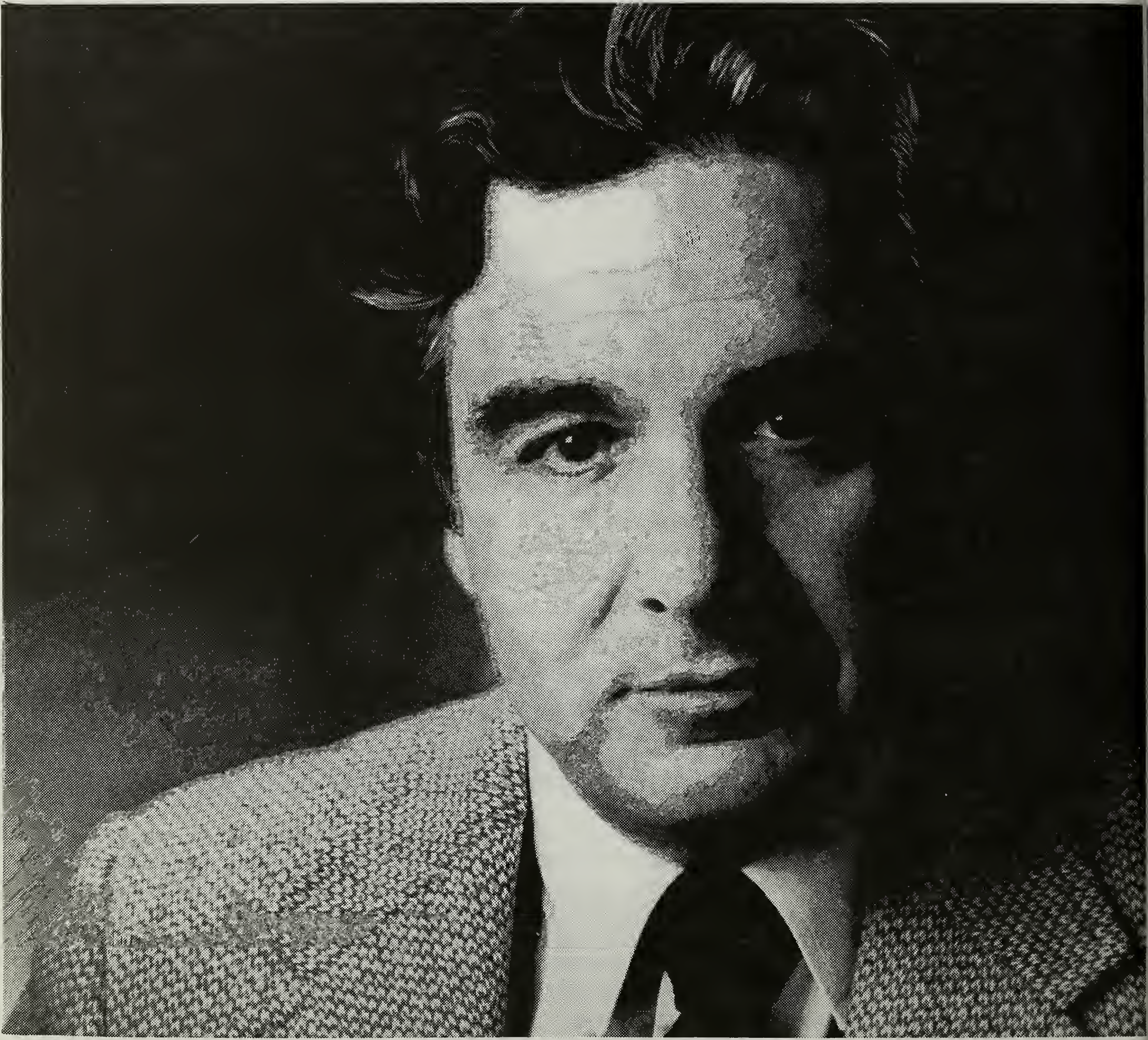
H.B. 5353 would have allowed chiropractors to perform school athletic team physicals and to be team physicians. It was never acted on by the Education Committee.

S.B. 924 would have allowed optometrists to use therapeutic drugs for certain diseases of the eye. This was never drafted, but was amended to another bill, passed by Appropriations, amended in the Senate, and referred to Judiciary, where it was killed.

Anthony P. Redmond, M.D.
President

"I'm accountable to my patients, not to an insurance company. That's just the way I operate."

—Dr. Vincent Catrini, General Surgery, Middletown, CT



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Vivian C. Feriola

1920-1991

ROBERT U. MASSEY, M.D.

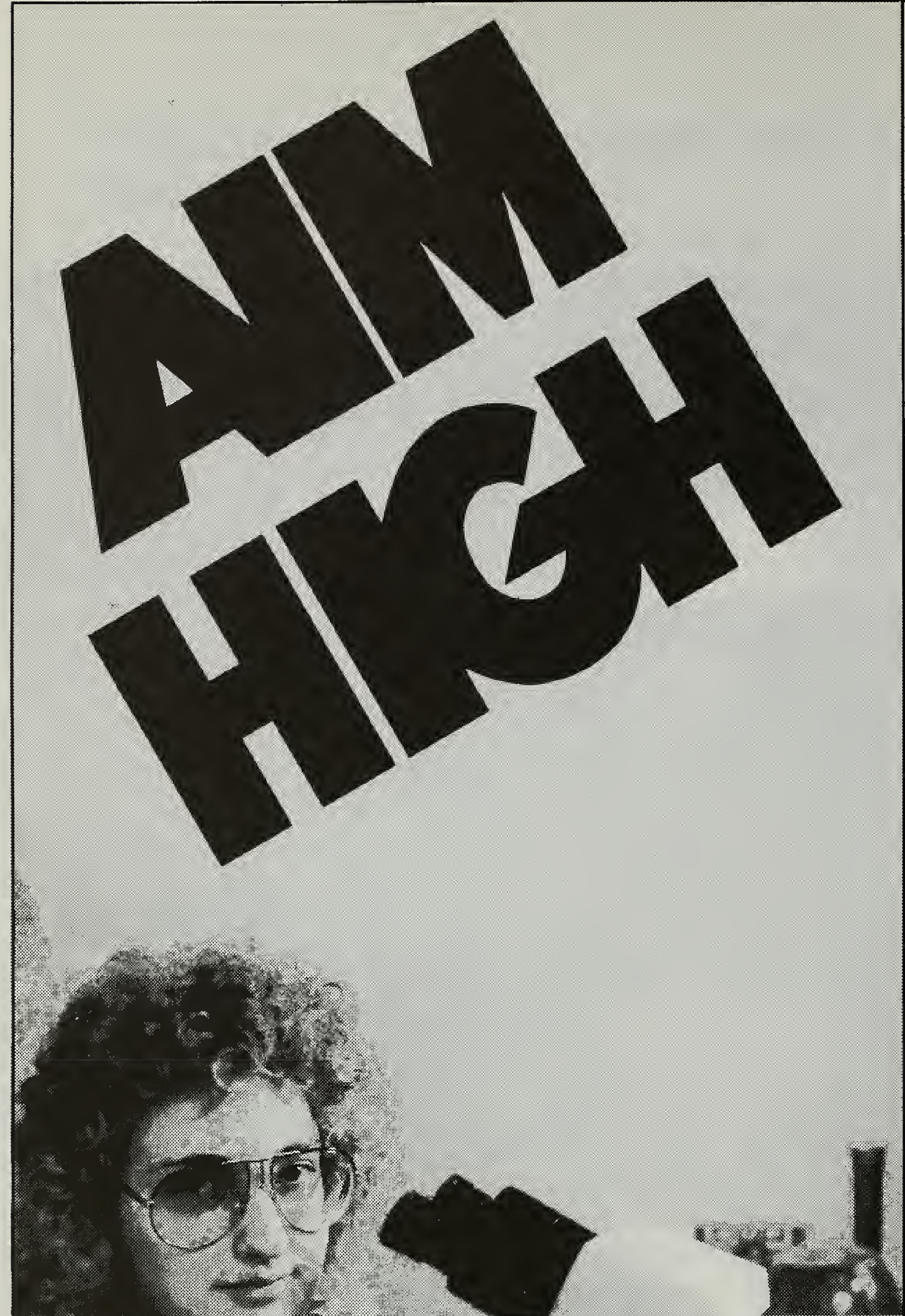
VIVIAN FERIOLA came to work for the Connecticut State Medical Society, and for *Connecticut Medicine*, in 1950, and for the next 41 years took responsibility for all those numberless details that go into the making of a monthly journal. I first met her in 1973, a few weeks after the editor, Dr. J. Alfred Fabro, had cajoled me into writing a monthly page for the *Journal*, "from the dean's office," he suggested, "about anything you'd like." Vivian had called me to say that my initial submission was too long, as I might easily observe by examining the page proof, and that I must shorten it by at least 100 words unless I intended it to spill over onto a second page in which case I must lengthen it. I set to work deleting adjectives and adverbs, unnecessary phrases, and generally tightening a manifestly loose-jointed composition. She called again to explain that the way I had chosen—crossing out words and phrases here and there—could be expensive (for the author!); why not take out one of the paragraphs, and she indicated the one that could be sacrificed without ever being missed. I hand-carried the final copy to her. After that each word was carefully counted, and the total neither exceeded 740 nor fell short of 680. Every month thereafter, close to the 15th, she would call to remind me that the page was overdue; the day after tomorrow would be soon enough.

In September 1986 I accepted the post of editor and began to work not only with but for Vivian Feriola. In one of our early conversations she remarked that publishing the *Journal* was simply a matter of paying close attention to details, and indeed she knew every one of them well and remembered them all, from receiving and acknowledging manuscripts, to keeping track of the reviewers' progress, handling the correspondence and angry phone calls from authors who had not yet seen their manuscripts in print, being certain that I completed my copy-editing in time for the printer, being sure that authors' names were spelled right and their titles and degrees shown correctly, and that the final proof-reading was completed on time. She wrote a deadline date in the corner of every piece of paper. She scanned the *JAMA* or the *New England Journal*, usually while eating lunch at her desk, or at home at night, looking for articles to suggest for reprinting or new layouts to try. Every month she thumbed through a dozen other state medical journals, the *MMWR*, the *Medical Letter*, or publications from the AMA and NIH. She brought in clippings from the *Register* or the New York *Times* that related to medicine or health policy. She looked after the advertising copy, spotted advertisements that might be in questionable taste, saw to it that the bills were paid, and paid attention to the advertisers' wishes about where their ads should appear. She "put the *Journal* to bed" each month, arranging the page layout, helping to select fillers, and being sure of the page count. She made up the annual index, and she proposed the annual budget. She provided the editor with tea and fruit, and did a hundred other things, looking after all the details, never thinking of credit for herself. "Just doing my job," she would say, "It's the way I was trained."

Vivian Feriola died in her sleep Thursday morning, 20 June. She had been busy at work all the day before, putting the June issue "to bed." Later she completed preparations, including purchasing the food, for a meeting of the Editorial Board that had been planned for Thursday evening, but was never held. Many Board members called or wrote; their sympathies and ours are now especially with her husband, Peter Feriola, and her brother, Leonard Conversi.

Assistant to the Editor until December 1987, Managing Editor since, Vivian will be missed by everyone in the offices at 160 St. Ronan Street, but most of all by Editorial Board members and all the others on the *Journal* staff who have depended upon her for so long. She served *Connecticut Medicine* faithfully for 41 of its 55 years with honest craftsmanship and painstaking care, but especially with pride, for it was her *Journal*.

ROBERT U. MASSEY, M.D., Professor, Division of Humanistic Studies in Medicine, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.



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AIR FORCE

The Month's Reading in Review

TIMOTHY B. NORBECK

- As reported in the *Wall Street Journal*, "Two recent events make it clear that on no issue does the intent of Congress and the intent of voters diverge more than on term limits"...In late May, 82 percent of the voters in Jacksonville, Florida voted to limit their City Council to eight years in office...When U.S. Senator Hank Brown (Colorado) recently proposed adding term limits to a campaign-financing bill, he lost on a 68-to-30 vote...
- Delegates to the annual meeting of the U.S. Chamber of Commerce registered 79 percent opposition to legislation that would force employers to choose between providing health insurance for their workers and paying a tax that would finance such coverage...Only 10 percent of those polled at the Chamber meeting expressed support for mandated health insurance.
- Nearly two out of three top U.S. business leaders polled by *Fortune* magazine called "skyrocketing" medical costs one of the worst problems facing American corporations...Some 35 percent of them went one step further and called the escalating cost of medical insurance the biggest problem they will confront in the 1990's...Despite these concerns, 69 percent of the CEOs were opposed to nationalized health care financed by U.S. taxpayers while 24 percent believed that such a move was necessary.
- Canadian tobacco manufacturers have urged their country's smokers to revolt against increased tobacco taxes which have raised the cost of a pack of cigarettes to $7 or more...The federal budget, approved in February, raised sin taxes and several provinces followed suit...A $2 million write-in protest campaign aimed at Prime Minister Brian Mulroney and Parliament has been initiated by the Canadian Tobacco Manufacturer's Council.
- By looking at college enrollment patterns in some 55 countries, University of Chicago and Harvard economists tested their theory that the practice of law can often interfere with the efficient workings of the economy and inhibit growth...Their studies reveal a strong positive relationship between engineering students and growth and a "negative effect of lawyers on growth."...Since the U.S. is the world's most litigious society, the researchers believe their study may shed light on America's lagging productivity..."Lawyers," the authors write, "are indeed bad, and engineers good, for growth."
- According to a recent study by researchers at San Jose State and Stanford Universities, over $2,900 could be saved per person per year in direct and indirect medical costs by improving specific health habits...The health habits of a group of retirees whose average age was 69 were analyzed...The researchers found that such factors as cigarette smoking, excessive drinking and obesity were significantly associated with higher medical costs.
- Participants in the NASA fitness program report significant health benefits...According to reports from the Dallas school system, absenteeism among exercising teachers dropped to an average of 5.3 days from 8.5 days per year, resulting in a savings of $452,000 for the school system.
- Half of all elderly nursing-home residents covered by Medicaid are "spend-downers," according to the Robert Wood Johnson Foundation...Spend-downers are those who have exhausted their personal assets to qualify for Medicaid...Of the more than 36,000 residents studied, 27 percent began their nursing home

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TIMOTHY B. NORBECK, Executive Director of the Connecticut State Medical Society.

stays as private-pay patients and spent down to Medicaid eligibility...Thirty-eight percent were eligible within 90 days and 55 percent within six months.

- *The New England Journal of Medicine* reports that more then 43 percent of all Americans reaching age 65 “are expected to enter a nursing home at least once before they die.”...Of these individuals, approximately 20 percent can expect to live five years or more in a nursing home at a cost of at least $25,000 a year.
- Medicaid is now the second largest line item in state budgets eating up 14 percent of revenues in 1990, up from 9 percent in 1980...By 1995, it is expected to grow to 17 percent of revenues.
- *The Los Angeles Times* reports that the chief of staff to U.S. Senator Sam Nunn (GA.) received more than $32,000 in consulting fees and expenses from Nunn’s campaign treasury during the past campaign cycle...Nunn’s treasurer told the *Times* that the money was for advice given during the campaign...Nunn was reelected and ran unopposed!

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Letter to the Editor

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TOBACCO SMOKE AND RISKS FOR NON-SMOKERS

To the Editor: In January, 1981, Hirayama published a landmark paper in which he found that non-smoking wives of men who smoked a pack or more of cigarettes a day had twice the lung cancer rate of non-smoking wives of men who did not smoke.[1] In July, 1981 I wrote an editorial in *Connecticut Medicine* on the effects of tobacco smoke on the non-smoker.[2] Smoke-filled rooms contain such carcinogens as N-nitroso-dimethylamine and benzo (a) pyrene which when inhaled cause the urine to be increasingly mutagenic in the salmonella/microsome assay.[3] In the past decade, Hirayama's study has been abundantly confirmed.[4] Last year Janerich et al reported that the risk of lung cancer among non-smokers was twice as high among those who as children or adolescents were exposed to smoking parents as among those who were not so exposed.[5] In December, 1990, The Environmental Protection Agency drafted a report estimating 3,800 cases of lung cancer a year caused in non-smokers by cigarette smoke. Employers now face a public health liability for passive smoking. A bus driver for the Melbourne Transit Authority has accepted 65,000 Australian dollars as compensation for his lung cancer caused by passive smoking. In the United States the tobacco companies are not protected by the Surgeon General's warning in the case of those who are forced to inhale second-hand smoke. This applies to heart disease as well as lung cancer. A non-smoking waiter in California, who had a heart attack, has been awarded about $85,000 in medical expenses by the State Compensation Insurance Fund. Where there's smoke, there will be law suits.

Raymond Yesner, M.D.

New Haven

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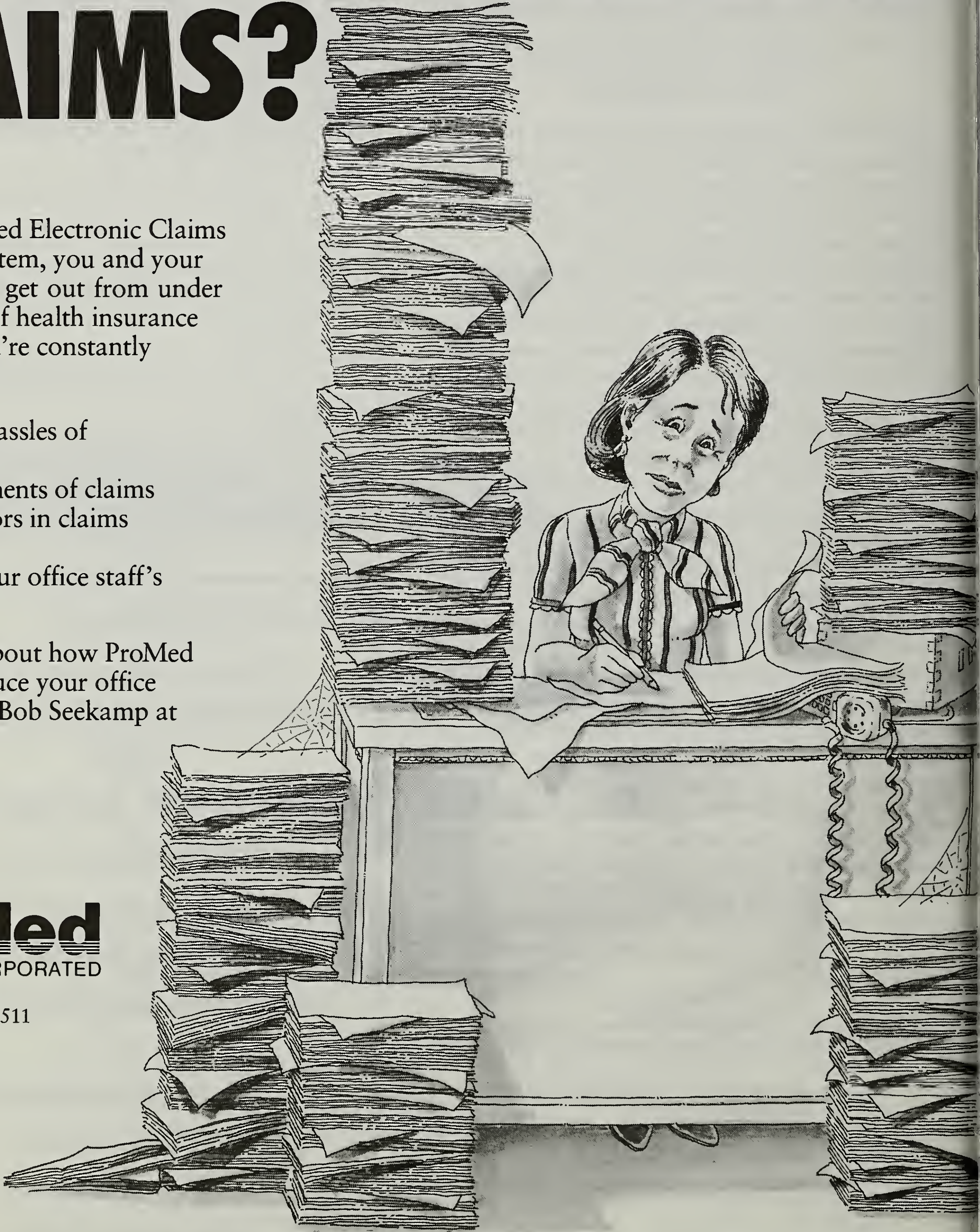

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From the Executive Director's Office

COUNCIL MINUTES

Thursday, June 13, 1991

Organizational Meeting

The organizational meeting of the Council for 1991-1992 was called to order by the President, Anthony P. Redmond, M.D. He welcomed the old and new councilors to the meeting and expressed his concern that we are divided in county and state membership and not united in the AMA and, therefore, have very little impact on opposing government intervention into medicine. He hoped that we could all be united and speak with one voice as we deal with business, insurance and government. Following his remarks he called for the nominations for Chairman and Vice-Chairman of the Council for 1991-1992. It was VOTED to elect Joseph C. Czarsty, M.D., Oakville, Chairman, and Joseph S. Sadowski, M.D., Hartford, Vice-Chairman.

Dr. Redmond called on Len Tomat, Executive Director of the Fairfield County Medical Association, who is retiring in September and was attending his last Council meeting, and asked him to say a few words. Mr. Tomat reminisced about his 21 years with organized medicine, six years with the Connecticut State Medical Society and 15 years with the Fairfield County Medical Association. He stated that many of the problems facing medicine 21 years ago are still facing medicine today, i.e. Medicare and third party payors. He informed the Council that he will be moving to Cape Cod.

It was VOTED to present Mr. Tomat with the chair he sat in originally in recognition of his services to the CSMS membership with proper inscription.

BUSINESS MEETING

Attendance

Present, in addition to the Chairman, Dr. Joseph C. Czarsty were Drs. Ahamed, Beck, Blake, Blum, Bobruff, Brooks, Cottle, Dardick, Deren, Eslami, Marvin Fox, Franklin, Freedman, Hollister, Kamens, Keating, McDonnell, Meridy, Orphanos, Petrie, Redmond, Sadowski, Sosa, Van Nostrand, Wetstone, Zeppieri.

Also present: Mr. Norbeck, Mrs. Lindquist, Mr. Brunell, Mr. Garofalo, Ms. Ballou, Mr. Tomat (FCMA), Mr. Coffey (HCMA), and Mr. Freberg (NHCMA).

Absent were: Drs. Brendan Fox, Hoskings, Lesnik, Parikh, Petro, Tesoro, Wolfson, Zanker.

Report of the President

Dr. Redmond reported that he attended the Massachusetts Medical Society meeting which was on the future of health care in the United States and heard presentations from Ted Cooper, M.D., the Chief Justice of the Massachusetts Supreme Court; Mr. Robert Maxwell, President of the AARP; Senator John Rockefeller, (West Virginia); Uwe Reinhardt, Economist; and Arnold Relman. M.D., Editor of the *New England Journal of Medicine*. He reported that many of the Connecticut hospitals are starting their own IPO's; this is the banding together of all local physicians and in order for any HMO, PPO to deal with them, they have to go through the IPO. Up to now physicians have decided how to treat patients; these IPO's will bring a change; the hospital will be telling the physician what he can do. He stated that as we go into this new stage of medicine we are going to have to be very careful because in the coming year physicians will be pulled along by the hospitals, communities, and government.

Legislative Review

Dr. Wetstone stated that our membership can feel confident that the funds allocated for the legislative program were well spent and that all concerned, including many of our physicians, did yeomen work in the legislative arena. One bill that required a great deal of attention was the optometry bill that would have allowed optometrists to use therapeutic drugs for certain conditions of the eyes. The bill was carefully followed through many channels and finally it was amended to require optometrists to be held to the same legal standard of care as opthalmologists. That required the bill to go to the Judicial Committee where it died. We can be certain that this bill will reappear next year.

Report of the Executive Director

Mr. Norbeck reported that he met with several members of the Dental Association who expressed an interest in meeting with officers of CSMS to discuss matters of mutual concern and will be writing a letter to CSMS requesting such a meeting. He reported further on Florida's Governor Lawton Childs' proposal to tax each physician $500 to help fund indigent care in Florida. The bill was quickly approved by the House Committee on Health Care, but appears to be dead now, due to an amendment which would require the Florida Supreme Court to collect a $1,000 assessment from each lawyer to help fund the public defender's office.

Mr. Norbeck brought to the attention of the Council a letter from the *Hartford Courant* requesting nominations for membership in a Community Focus Panel. This advisory group reflects greater Hartford's rich diversity and provides *Courant* editors with feedback on their coverage of the region. It was VOTED to suggest the following names for membership on this group: Katherine Ill, M.D., Roger Beck, M.D. and Neil Brooks, M.D.

Three letters were circulated among the Council members, one from Dr. Warren Emley, Delegate from New Hampshire, commending CSMS on its efficiency in running their House of Delegates, one from the Salvation Army thanking the members for their contribution to them from the Charitable Trust Fund and another from one of the students winning the science award. (AMB 6/13/91 "B")

Appointment of Committee on Alcohol and Other Drug Dependency Education

At the House of Delegates meeting, it was voted that the CSMS Council appoint up to 12 members and name the chairman thereof and that these names be submitted to the next meeting of the House of Delegates for confirmation. It was VOTED that the Chairman of the Council appoint the committee and the following members were appointed:

Peter O. Rostenberg, M.D., Danbury, Chairman
Albert Browne-Mayers, M.D., Willimantic
Harold Engelke, M.D., New London
Mark Kraus, M.D., Waterbury
William Lyons, M.D., Southbury
Duncan MacMaster, M.D., Southbury
James E. O'Brien, M.D., Wethersfield
Charles Riordan, M.D., New Haven
Richard Schottenfeld, M.D., New Haven
Robert Walzer, M.D., Norwalk

Report of Ad Hoc Committee on AMA Membership Development

Stewart J. Petrie, M.D., AMA Delegate, reported that the Ad Hoc Committee had met just prior to the Council meeting and reviewed a statistical list of the percentage of AMA members in each county, in the House of Delegates and in the Council. It was noted that 78% of the members of the Council were members of the AMA and it was felt that as medical leaders they should have unified membership. It was also reported that Connecticut was the only New England State that did not mandate unified county and state membership and one of eleven states in the country who did not have unified county and state membership. Following discussion, it was VOTED:

(a) That an amendment to the CSMS Bylaws be submitted to the House of Delegates at the semi-annual meeting that would require that all members of the Council not only be members of the county and state, but also of the AMA.

(b) That an amendment to the CSMS Bylaws be submitted to the House of Delegates at the semi-annual meeting that would require all county delegates to the House of Delegates not only be members of the county and state, but also of the AMA.

(c) That the Council recommend to the county associations that their bylaws be amended to require all county members to become CSMS members.

(d) That staff develop a plan to contact doctors who paid their 1989 AMA dues and not the 1990 AMA dues.

(e) That staff prepare a recommendation as to how to encourage residents and student members to become members of the AMA and present the plan to the Council at its next meeting.

State Commissioner of Health

At the invitation of the Council, Susan S. Addiss, M.P.H., State Commissioner of Health, joined the Council to share her concerns with them. She stated that she had already met with several of the county associations and specialty sections, which has given her an opportunity to meet many physicians. She stated that at the present time, they are deliberating on the reorganization of the health department mostly to centralize administrative, business, personnel and grant management functions which have gotten decompartmentalized. She reported that in their dealing with the legislature they have had some victories but also some losses. They have already laid off 23 employees and do not know whether there will be any more layoffs. That will depend upon the budget which is adopted. Of interest to physicians is the fact that in the health department budget is an extra million dollars to be given to community health centers for the care of the uninsured. Also proposed in the budget is a million dollars for bonding of community health centers which will enable them to make renovations and structural changes they would need to handle the extra people they would be going out and recruiting. There is also proposed in the budget three and a half million dollars in bonding to construct appropriate facilities for AIDS patients. She reported that in the department there is an increased focus in the toxic hazard unit which will be responding to requests from work sites to investigate possible exposures to toxic substances. It was reported that the department will be receiving three physicians from the Centers for Disease Control which will be working in various aspects of health care in the department. She also informed the Council that the department has submitted an application to NCI for a three and half million dollar grant for funds to promote both mammography clinical exams and pap screening exams for at risk women, i.e. low income, uninsured, and uninformed. She further stated that one of her priorities is maternal and child health care. Dr. Czarsty thanked Commissioner Addiss for her informative presentation and for taking the time out of her busy schedule to address the Council and that she had an open invitation to address the Council.

American College of Surgeons Newsletter

Dr. Ahamed brought to the attention of the Council an item in the newsletter pertaining to the possibility of reorganizing the CSMS Section on Surgery that had been disbanded several years ago. The Chairman of the Council appointed Drs. Robert Cottle and Sultan Ahamed to pursue the differences between the American Board Surgeons and the American College of Surgeons and to decide whether or not they wish to request authorization to reinstitute a CSMS Section on Surgery.

Communication Re M.D. Health Plan

A letter was received by the Chairman of the Council from a member regarding the CSMS-IPA reimbursement policy. The letter had been referred to the IPA and CSMS was informed that the physician's comments were to be discussed at the June Board meeting and that they had contacted the physician and informed him that the management was recommending the CSMS-IPA policy be changed to be consistent with the physician's request. Dr. Guy Van Syckle, Medical Director of M.D. Health Plan, joined the Council and informed them that occasionally the problem arises when a physician treats a patient, who at the time of treatment was verified as being covered under M.D. Health Plan, but when the claim reaches the M.D. Health Plan, the records indicate that payment was discontinued and thereby the payment was denied. This does not happen very often and after considering the letter submitted to them, the IPA Board has recommended to the M.D. Health Plan that if proper certification is made of a patient's coverage at the time of treatment, the physician will be paid, regardless of the fact that it is later determined that the premium was not paid.

Dr. Van Syckle gave a brief statistical update concerning membership, physician participation and claims.

Communication from Connecticut Academy of Family Physicians

It was VOTED to refer the following action taken by the Connecticut Academy of Family Physicians to the CSMS Committee on Legislation:

> "That the Connecticut Academy of Family Physicians co-sponsor with the Connecticut State Medical Society legislation to be introduced to the 1991 Session of the Connecticut General Assembly which will ban smoking in all public buildings.

Committee on Emergency Medical Service

It was VOTED to endorse the concept set forth in the "Guidelines For Do Not Resuscitate Orders" developed by the Committee on Emergency Medical Service and to instruct staff to take whatever steps necessary to implement them.

Committee on Perinatal Morbidity and Mortality

The Council reviewed the report of the subject committee which responded to the Council's request to develop the cost of a completely unbiased study of neonatal and maternal service needs in Connecticut and to report back to the Council as to procedure and cost. The Committee's report stated that due to the fact that conditions seem to be easing, the Committee recommends that a hold be put on the study. It was VOTED to receive the report for information and refer it to the American College of Obstetrics and Gynecology.

CSMS Smoking Cessation Workshops

It was VOTED to approve the recommendation of the Committee on Public Affairs to co-sponsor with the American Cancer Society a series of workshops. CSMS's participation will be to urge its network of Directors of Medical Education to schedule a workshop in each of the 35 community hospitals accredited for CME by CSMS in the coming months. In addition, a schedule of these meetings will be published to provide maximum opportunity for practitioners to attend conveniently.

Proposed Dates for Semi-Annual and Annual Meeting

It was VOTED to approve the following dates:

Semi-Annual Meeting, Thursday, November 21, 1991 - Ramada Inn, Meriden

Annual Meeting, Wednesday, May 6, 1992

Dates for Future Council Meetings

Wednesday, August 14, 1991
Thursday, September 19th, 1991
Wednesday, October 23, 1991

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on Thursday, June 13, 1991. Detailed minutes of the meetings are on file at 160 St. Ronan Street, New Haven, for perusal by any interested members of the Society.*

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LACH, FRANK E., University of Maryland, 1941. Doctor Lach was an obstetrician and gynecologist in New Haven and Milford for 45 years. He was a member of the New Haven County Medical Association and the Connecticut State Medical Society. Doctor Lach died 15 June 1991, at the age of 76.

LOVELESS, MARY H., Stanford University, 1925. Doctor Loveless was an Immunologist in San Francisco and Westport for many years. Doctor Loveless was a member of the Fairfield County Medical Association and the Connecticut State Medical Association. Doctor Loveless died 2 June 1991, at the age of 92.

RENTSCH, SAMUEL S., University of Michigan, 1923. Doctor Rentsch was a surgeon for nearly 50 years in the Derby area. He was a member of the New Haven County Medical Association, Connecticut State Medical Society and the American Medical Association. Doctor Rentsch served on several committees of the CSMS. He died 8 June 1991, at the age of 98.

SYZ, HANS, Geneva Medical School, 1921. Doctor Syz was a Psychiatrist in the Westport area for many years. Doctor Syz, was a member of the Fairfield County Medical Association, Connecticut State Medical Society and the American Medical Association. Doctor Syz died 29 May 1991, at the age of 96.

THOMSON, ARCHIBALD W., Jr., Cornell 1943. Doctor Thomson was an obstetrician and gynecologist in Middletown for the past 40 years. Doctor Thomson was a member of the Middlesex County Medical Association and the Connecticut State Medical Society. Doctor Thomson, who had served on several committees of the CSMS, died 26 May 1991, at the age of 73.

WILLIAMS, EDWARD E., Columbia University College of Physicians and Surgeons 1923. Doctor Williams practiced in Naugatuck for many years before his retirement. He was a member of the New Haven County Medical Association, Connecticut State Medical Society and the American Medical Association. Doctor Williams died 12 June 1991, at the age of 94.

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Practices Around Periodic Cancer Screening by Physicians in Primary Care Specialties

H. ANDREW SELINGER, M.D., DAVID I. GREGORIO, PH.D., M.S., AND LISA A. STRELEZ, B.A.

ABSTRACT—Questionnaires and information packets were distributed to 121 physicians in primary care specialties in central Connecticut to ascertain how periodic cancer screening is performed and monitored. Results of a baseline survey of 52 respondents (51% of active practitioners) are presented here. Only one quarter of respondents noted some formal mechanism in place within their practice to encourage periodic screening of patients. We estimate that only 20-30% of physicians complete cancer screening activities during routine office visits, although respondents noted this to be the most common type of patient encounter. Relatively few physicians reported reliance on either memory aids (17%) or office staff (20%) to prompt screening recommendations. Three of four respondents noted that the sole mechanism they utilize to initiate cancer screening is physician chart review. Likewise, follow-up of scheduled screening activities relies predominantly on chart review or patient review at the time of a subsequent office visit. Use of "tickler files" or scanning of computerized records are considerably less common practices. These data suggest that physicians in primary care practices often function without specific mechanisms to facilitate performance and improve follow-up of health promoting activities.

Introduction

PHYSICIANS, like the public-at-large, generally subscribe to the value of preventive health practices. One recent survey of primary care practitioners published in the *New England Journal of Medicine* found consensus that "eliminating smoking, avoiding excess calories, using seat belts and eating a balanced diet were 'very important' in promoting the health of the average person."[1] Data recently published by the American College of Surgeons (ACS) indicated that physicians are increasingly receptive to cancer detection and cancer prevention counseling within their practices.[2] Of some 1,000 physicians questioned, 80% reported that they do more screening of asymptomatic patients for early detection of cancer now than they did five years ago.

Despite beliefs in the efficacy of cancer prevention counseling and early cancer detection procedures, studies that have looked at implementation of early cancer detection practices in primary-care settings generally have found poor compliance by physicians. One retrospective study of a large university-based general internal medicine practice found performance rates for seven principle cancer screening tests (excluding the Pap smear) to be significantly below ACS guidelines.[3] Reasons cited by physicians for failing to comply with recommendations included provider forgetfulness, lack of time, inconvenience, and logistical difficulties. Selinger et al found that 56% of female patients over age 55 who were treated at a large, urban family practice had no record of mammograms over a five-year period.[4] A survey of primary care physicians in New York City (N=120) found only two of five respondents regularly followed guidelines regarding the use of sigmoidoscopy in their practices, while only one of five (21%) regularly followed guidelines for screening mammography. Current ACS data, although more optimistic, show similar gaps between performance and recommendation of screening

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Reprint requests to: The Family Medical Group, 1158 Farmington Ave, Bristol, CT 06010 (Dr. Selinger).

A version of this paper was presented to the Centers for Disease Control Annual Meeting, Prevention 90: Assuring the Public Health, April 1990, Atlanta, Georgia.

procedures.[5] Roughly one-half of respondents (45%) noted that patients are interested in cancer-prevention counseling, although a majority of physicians (56%) acknowledged that they lacked educational resources needed for an effective job.

We speculate that additional barriers to appropriate cancer screening by physicians in primary care settings include features of medical office operations, that is, the way and when doctors "see patients," and the medical record procedures they utilize for tracking patient care. Styles of practice and specialization by primary care physicians, for example, may limit what screening (if any) is done, as well as how and when the procedure would occur. Similarly, the extent of office automation could influence a physician's access to, and use of, aids to prompt periodic screening and follow-up examination results.

To examine these issues, a study of cancer screening in office-based practices was undertaken under the auspices of the American Cancer Society, Connecticut Division (ACS). The initial phase of research reported here surveyed physicians about the place of cancer screening and health promotion within their practices. Questions specifically addressed when and how cancer screening examinations are performed or recommended for their patients, and the mechanisms in place within their practices for recommending, recording, and following up examination results. Subsequent phases of the project involve the distribution of a memory aid (ie, flowsheet) to practitioners designed to facilitate in-office cancer screening and health promotion.

Methods

Physicians practicing internal medicine, obstetrics and gynecology, and family or general medicine within the service area of the New Britain Conn. Chapter of the ACS were the target population for our study. Rosters of physicians were obtained from the Connecticut State Medical Society and the ACS, as well as through inquiries to appropriate departments at the three regional hospitals. All physicians identified in this manner (N=123) were contacted by mailed questionnaire, along with a cover letter stating the purpose of the solicitation. It was subsequently determined that 22 physicians were either no longer in practice or decreased.

Questionnaires were developed with input from physicians, and were reviewed by all appropriate department chairpersons at each of the hospitals before the instrument was distributed to practitioners. Items addressed the background of respondents (years in practice, specialty); the size and characteristics of their individual practices (type of practice arrangements, estimated numbers of patients served, portion of caseload receiving primary care, patient characteristics). Physicians were further questioned about their attention to routine cancer screening procedures within their practices (procedures addressed, barriers to performance of examinations, etc.); and medical record keeping systems in their offices (mechanisms to prompt performance and follow-up of cancer screening activities).

Table 1
Cancer screening/health promoting practices of primary care physicians.

Procedure	*Done within my practice*	*Referred outside my practice*	*Not addressed in my practice*
Health counseling	88%	0%	12%
Periodic physical exams	90%	2%	8%
Digital rectal exams	92%	0%	8%
Stool occult blood testing	88%	4%	2%
Proctosigmoidoscopy	33%	39%	28%
Physical breast examination	94%	0%	6%
Mammography	6%	88%	6%
Pelvic examination	76%	14%	10%
Teaching breast self-examination	59%	12%	29%
Endometrial tissue sampling at menopause	14%	24%	62%

A total of 52 respondents (51% of active practitioners within the target area) were reached through the initial or follow-up mailings. Of this number, roughly two thirds (n=34) were specialists of internal medicine, while 12 were obstetrician and gynecologists (23%), and six (12%) specialized in family or general medicine. Fifteen respondents (29%) reported being solo practitioners, with the remainder (n=37; 71%) work in group practice arrangements. Estimates by physicians regarding the size of their practices suggest an average caseload of 2,300 patients, yielding an approximate total of 120,000 patients seen by these care givers in the aggregate (actual number may be somewhat smaller given persons seen by more than one primary-care specialist).

Summary measures of questionnaire items (frequencies, percentages, etc.) are presented. Although subtle response biases, which could not be assessed given the number of questionnaires returned, may be present here, we believe that respondents were typical of other primary-care practitioners working within the targeted area, and quite possibly of those in similar practices elsewhere. Comparison of physicians who did and did not respond to the survey failed to demonstrate observable differences between groups. Similarly, comparisons among physi-

Table 2

Occurrence of screening activities† by type of office visit.

	Type of office visit			
Screening Activity	*Acute visit*	*Routine visit for established illness*	*Comprehensive periodic physical examinations*	*Preventive care*
Chart review for "past-due" screening activities	40%	44%	42%	27%
Provide health counseling	19%	56%	54%	38%
Schedule screening activities	15%	33%	48%	25%
Complete screening activities	2%	25%	58%	25%

†Percentages reflect the proportion of study subjects (N=52) who responded affirmatively to question.

cians reached through successive mailings did not reveal differences among groups.

Results

Overall, physicians noted that many cancer screening and health promoting activities were available within their practices for patients, with most others available through referral to other practitioners (see Table 1). More than four of five physicians offered health counseling, periodic physicals, digital rectal examinations, stool occult blood tests, and physical breast examinations to their patients. Somewhat fewer provided pelvic exams (76%) or taught breast self-examination (59%) to patients. Referral of women for mammography was common for nine of 10 respondents.

Relatively few physicians indicated that particular procedures were not addressed within their practice. As reported in other recent surveys,[2] sigmoidoscopy remained a cancer screening practice in limited use. Approximately one third of respondents performed sigmoidoscopies, while nearly an equal proportion (28%) did not address the procedure within their practices. Similarly, endometrial tissue sampling at menopause and breast self-examination instruction were procedures not routinely addressed (62% and 29%, respectively).

Whether physicians complete or schedule screening examinations appeared to depend upon the reason why patients were seen by their physician (see Table 2). Routine office visits for care of established illnesses, although judged the most common type of patient encounter by three of five respondents, were generally not occasions when physicians either complete or schedule cancer screening examinations. Only one quarter of respondents indicated that they perform screening examinations, and one third reported that they scheduled screening activities during those times. Roughly one half of respondents reported such encounters to be suitable occasions for general health counseling.

Respondents indicated that they were not likely to address cancer screening issues during patient visits for acute illness; only one respondent reported completing screening examinations during such encounters. Referral of patients for screening was likewise an uncommon outcome of such an encounter, and only seven of 52 indicated that they use such occasions for scheduling appointments for screening exams. Even preventive care visits were not likely encounters for doing or arranging for cancer screening activities. Rather, physicians reported that cancer screening was most often a part of patient visits for periodic physical examination. Roughly three of five respondents noted that screening was done during such visits. However, physicians acknowledged that comprehensive physical examinations represent only a small portion of total patient encounters.

What specific mechanisms do physicians utilize to assure that cancer screening procedures which are customarily addressed in the course of patient care are either carried out or referred to others? Our findings suggest that cancer screening is very much a physician-driven activity; involvement of office staff, the use of memory aids, or office automation to prompt screening is extremely limited among the physicians questioned (see Table 3). For example, only two of 52 respondents (4%) indicated that they currently utilized computerized medical records with a programmed trigger to identify patients for periodic screening. It is equally uncommon for the clinical office staff to be responsible for flagging patient charts for screening (N=4; 8%) or to schedule such activities (N=6; 12%). Use of a checklist in a patient's medical record to remind physicians about screening was reported by only seven respondents (13%). In total, only 13 of 52 respondents (25%) noted some formal mechanism in place within their practice to encourage periodic cancer screening of patients. On the other hand, three quarters of respondents (N=39) noted that chart review at the time of office visits was the principal mechanism they employed to prompt screening of patients.

For those procedures that physicians indicated are referred outside their practices, how do they monitor such referrals and follow up completed test results? Follow-up of patient referrals to confirm the completion of examinations was also found to rely heavily upon physician initiative. One third of respondents indicated that chart review at the time of the next patient encounter was the principle means for following up test results; roughly the same proportion noted that consultation of patients was important in evaluating follow-up activities. Relatively few respondents utilized a standardized mechanism (ie, tickler files, periodic record scans, etc) in this regard.

Discussion

Physician practice patterns identified during our study suggest that certain office procedures may be obstacles to effective cancer screening in the ambulatory setting. Consistent with other recent surveys,[2,6] these respondents endorse most cancer screening and health promoting activities and make them available to patients within their practices or through referral. They generally endorse ACS cancer screening guidelines and find them helpful in their practices. However, respondents to our survey indicated that scheduling and completing screening examinations occur primarily during the comprehensive examinations which comprises only a small percentage of total patient encounters. With only one exception (ie, health counseling), less than one half of physician respondents reported that they addressed cancer screening issues during the bulk of their patient encounters.

Screening activities need to be increased during acute and routine office visits. This is not a new concept and has been suggested by others. Medical visits for nonacute and acute conditions should be viewed as opportunities to inquire about screening histories, and to encourage screening for cancer.[7] If not done, most patients, although seen periodically by their physicians, may nonetheless have age and gender appropriate indications for cancer screening that go unaddressed. This has implications for diminishing the quality of care and increasing professional liability.

The primary care office is a very busy place. A physician typically sees 100 to 120 patients per week in the ambulatory setting. Respondents to our survey reported that acute and routine visits last approximately 14 minutes and physicians comfortably address one to two patient care issues during this interval (data not presented). Phone calls are taken, tests ordered, prescriptions written, appointments scheduled, and procedures performed! Clinical and administrative support staff assist in these tasks and, in sufficient numbers, are essential for an office to function properly. Over-head costs in the primary-care office often average 50% or greater and much of this is for staff salaries. Yet, in our respondent group, screening mechanisms are primarily within the physician's domain. Only in approximately 10% of physician offices are staff empowered to identify patient charts where cancer screening is indicated, or to initiate screening activities. Why? Although not addressed in our study, we speculate that a combination of factors are relevant: the traditional model of medical office operations with strict separation of duties and levels of responsibility; lack of awareness that screening needs are often unaddressed, and the physician's desire to be the sole decision-maker for the patient's health-care needs. In this age of developing national patient care guidelines and community-wide "standards of care," physicians need to define clearly the standard of care to be provided within their office and then work together with staff to make it a reality.

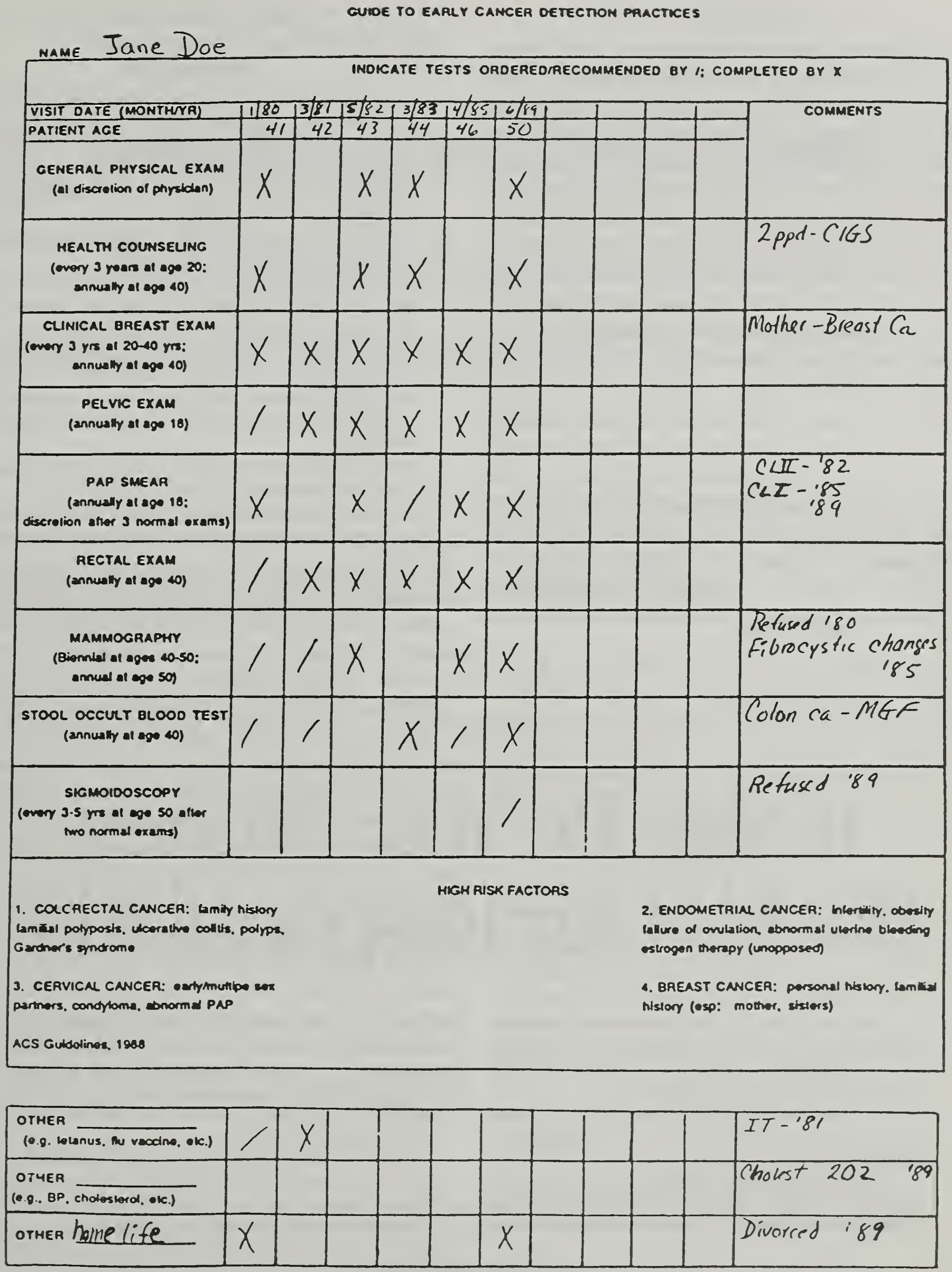
Table 3
Mechanisms used by physicians to prompt screening and test follow-up†.

Screening mechanisms	#	%
Use of a checklist	7	13
Programmed "trigger" flags charts	2	4
Office staff schedules activity	4	8
Office staff flags charts	6	12
Chart review at time of office visit	39	75

Follow-up mechanisms	#	%
Scan computerized records/checklist	1	2
Use of "tickler file"	4	8
Ask patient about exam at next visit	18	35
Review patient record at next visit	19	36

Few physicians addressed screening during noncomprehensive visits, or indicated use of a chart organizer for their patient care records. More work needs to be done to identify the barriers that exist to effective cancer screening and to prioritize their significance. McCusker et al, has suggested an important determinant of the use of early detection techniques for cancer may be the quality of the physician-patient relationship, including demonstration of the physician's concern with the importance of early detection.[8]

Busy physicians cannot perform according to their own ideals without some form of mechanical aids. Other fields have long recognized this and provide memory aids. Check lists/flowsheets are most suitable for reminding about required interventions that apply to a large portion of one's population.[9] Few physicians (13%) reported use of a chart-based flowsheet and even fewer use a computerized recall system (4%) or manual tickler file (8%).



GUIDE TO EARLY CANCER DETECTION PRACTICES

NAME Jane Doe

INDICATE TESTS ORDERED/RECOMMENDED BY /; COMPLETED BY X

VISIT DATE (MONTH/YR)	1/80	3/81	5/82	3/83	4/85	6/89					COMMENTS
PATIENT AGE	41	42	43	44	46	50					
GENERAL PHYSICAL EXAM (at discretion of physician)	X		X	X		X					
HEALTH COUNSELING (every 3 years at age 20: annually at age 40)	X		X	X		X					2ppd-CIGS
CLINICAL BREAST EXAM (every 3 yrs at 20-40 yrs: annually at age 40)	X	X	X	X	X	X					Mother-Breast Ca
PELVIC EXAM (annually at age 18)	/	X	X	X	X	X					
PAP SMEAR (annually at age 18: discretion after 3 normal exams)	X		X	/	X	X					CLII-'82 CLI-'85 '89
RECTAL EXAM (annually at age 40)	/	X	X	X	X	X					
MAMMOGRAPHY (Biennial at ages 40-50: annual at age 50)	/	/	X		X	X					Refused '80 Fibrocystic changes '85
STOOL OCCULT BLOOD TEST (annually at age 40)	/	/		X	/	X					Colon ca-MGF
SIGMOIDOSCOPY (every 3-5 yrs at age 50 after two normal exams)						/					Refused '89

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4. BREAST CANCER: personal history, familial history (esp: mother, sisters)

ACS Guidelines, 1988

OTHER ______ (e.g. tetanus, flu vaccine, etc.)	/	X									IT-'81
OTHER ______ (e.g., BP, cholesterol, etc.)											Cholest 202 '89
OTHER home life	X					X					Divorced '89

Figure 1
Chart-based flowsheet for periodic cancer screening/health promotion.

Flowsheet and reminder systems have been studied in clinical trials. Davidson et al, in a large university-based general internal medicine practice, documented the following increases in performance when a nurse initiated health maintenance flowsheets and reminder systems were introduced: stool exams for occult blood 32 to 47%; breast examinations 29 to 40%; influenza immunizations 18 to 90%.[10] Our inquiry into the use of a chart-based flowsheet or similar memory aids to prompt, track, and follow up cancer screening and health promoting activities revealed that few practitioners currently utilize such devices.

Conclusion

Office operations play an important role in facilitating effective cancer screening in the ambulatory setting. Our sample size was small. This study will be repeated with a larger physician group to determine if our findings are reproducible. Nevertheless, the value of well designed office protocols in providing patient care cannot be minimized. Physicians and their staff need to work together through a coordinated effort to enhance the delivery of health promoting and cancer early detection services. Training to this end should take place during the residency years so that good habits are developed early in a physician's career and reinforced later through regular continuing medical education.

We have developed a chart-based flowsheet checklist to assist primary-care physicians in conducting periodic cancer screening of their patients (see Figure 1). The instrument, developed with input from several practicing physicians, requires little effort for effective use, and can readily be modified for additional purposes. It has been successfully pilot tested in a large family medicine practice. To date, the flowsheet checklist has been distributed to roughly 500 practitioners in Connecticut. We hope to report on these results in future issues.

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Pathologic Stage I and II Hodgkin's Disease

Long-Term Results at Three Connecticut Hospitals

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ABSTRACT—Three radiation therapy departments in Connecticut (Uncas on Thames Hospital, Norwich; Yale-New Haven Hospital, New Haven; and the Hospital of Saint Raphael, New Haven) have consistently used the strategy of staging laparotomy with splenectomy for clinical stage I and II Hodgkin's disease patients with primary radiation therapy as initial therapy for most pathologic stage (PS) I and II patients. From 1971 through 1986, 239 PS I and II patients were treated at these three institutions and 94% received radiation therapy alone as initial treatment. With a minimum follow-up time of one year and a maximum follow-up time of 18 years (mean: 7.3 years), only 19 (8%) of the 239 patients have ultimately died of Hodgkin's disease. Two factors were responsible for the low death rate due to Hodgkin's disease: 1) 176 patients (74%) went into complete remission following initial therapy and did not experience a relapse; and 2) 63 patients relapsed following initial therapy; however, subsequent salvage therapy was successful in 44 (70%) of these 63 patients. The overall 10-year and 18-year survival rates were 81% and 78%, respectively. Staging laparotomy with initial radiation therapy for most PS I and II patients remains an important and highly successful strategy for Hodgkin's disease.

Introduction

MANY cancer centers recommend staging laparotomy and splenectomy for most clinical stage (CS) I and II Hodgkin's disease adult patients.[1] This approach is based on two fundamental paradigms: 1) The staging laparotomy (SL) provides important information about the extent of disease which cannot be obtained with clinical staging. Most studies document that a SL changes the CS to a higher pathologic stage (PS) in approximately 25%-36% of all cases.[1,2,3] 2) Primary radiation therapy is the treatment of choice for most PS I and II patients. Chemotherapy or combined modality therapy (chemotherapy plus radiation therapy) is reserved as salvage therapy for primary radiation therapy patients who relapse. At least one randomized trial has verified the superiority of using primary radiation therapy (RT) compared to standard MOPP chemotherapy (nitrogen mustard, vincristine, procarbazine, and prednisone) for PS I and II patients.[4] This study documented equivalent five-year survival and disease free (NED) survival for RT versus MOPP but with less severe treatment complications and more successful salvage therapy in the RT group.[4]

Some CS I and II adult patients do not require laparotomy. For example, CS I and II patients who present with large mediastinal masses do not need a SL since most of these patients will be treated with combined modality therapy and the results of the SL will not influence treatment.[5,6] In addition, CS IA female patients and CS IA male patients with lymphocyte-predominant histology or high neck disease may not need a SL due to the less than 10% probability that such a procedure will be positive.[1]

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Table 1

Clinical Features of the PS I & II Hodgkin's Disease Patients

Total Number	239	
Males/Females	132/107 (1.2)	
Age: ave./median	28/27 (range: 9-59)	
Stage:		
IA	58	(24%)
IB	5	(2%)
IIA	138	(58%)
IIB	25	(10%)
$\mathrm{II_eA}$	11	(5%)
$\mathrm{II_eB}$	2	(1%)
Pathology:		
NSHD	185	(77%)
MCHD	35	(15%)
LPHD	18	(7.5%)
LDHD	1	(0.5%)
Initial Therapy:		
S (TNI)	213	(89%)
IF/EF	12	(5%)
IF/EF+Chemo	9	(4%)
S (TNI)+Chemo	5	(2%)

Key: NSHD-Nodular sclerosing; MCHD-Mixed cellularity; LPHD-Lymphocyte predominant; LDHD-Lymphocyte depleted; S(TNI)-Total nodal or subtotal nodal radiation; IF/EF-Involved or extended field radiation; Chemo-Combination chemotherapy.

Pediatric and geriatric patients represent two other groups of CS I and II Hodgkin's disease patients who may not require SL because of both the increased morbidity from SL and a difference in treatment philosophy for these two patient groups.[7,8]

Despite the documented success of SL in conjunction with RT for most PS I and II Hodgkin's patients,[9] some physicians have raised legitimate questions about the need for SL in the management of early stage disease. These questions are based on several factors: first, although the mortality from a SL is less than 0.4%, the total number of nonfatal acute and long-term complications in adults can vary from 3% to 10%.[1,3] Therefore, if other strategies can be found that avoid the SL without compromising survival, this may decrease the overall morbidity and inconvenience for the patient. Second, newer combinations of chemotherapy such as ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine) appear to be at least as effective as MOPP but with less toxicity.[10,11] If chemotherapy was used as primary treatment for early Hodgkin's disease, this would eliminate the need for a SL. Finally, several recent clinical trials at Stanford University comparing involved field radiation plus chemotherapy (either MOPP or PAVe: procarbazine, alkeran, vinblastine) versus standard total nodal or subtotal nodal RT for PS I and II patients have been interpreted to suggest that involved field radiation therapy plus chemotherapy can be used without the necessity of a SL in early Hodgkin's disease.[11]

Therefore, based on the considerations discussed above, it is appropriate that the precise role of the SL and RT for early stage Hodgkin's disease continues to undergo reexamination and redefinition. One of the most important aspects of this reevaluation process is the documentation of the long-term results of the strategy of using SL for CS I and II Hodgkin's patients and subsequent RT for most PS I and II patients (SL+RT). For this reason, we have analyzed the long-term results from the radiation therapy departments at three Connecticut Hospitals which have consistently followed the (SL+RT) philosophy for over 15 years.

Methods

From 1 January 1971 through 31 December 1986, 521 patients with a diagnosis of Hodgkin's disease were evaluated at three radiation therapy centers in Connecticut: Uncas on Thames Hospital, Norwich; Yale-New Haven Hospital, New Haven; and the Hospital of Saint Raphael, New Haven. The radiation therapy charts of these 521 patients were retrospectively reviewed. All patients were staged according to the Ann Arbor classification system.[12] During the 15 years covered in this study, all three institutions generally followed a policy of: 1) SL for early CS disease and 2) RT as initial therapy for

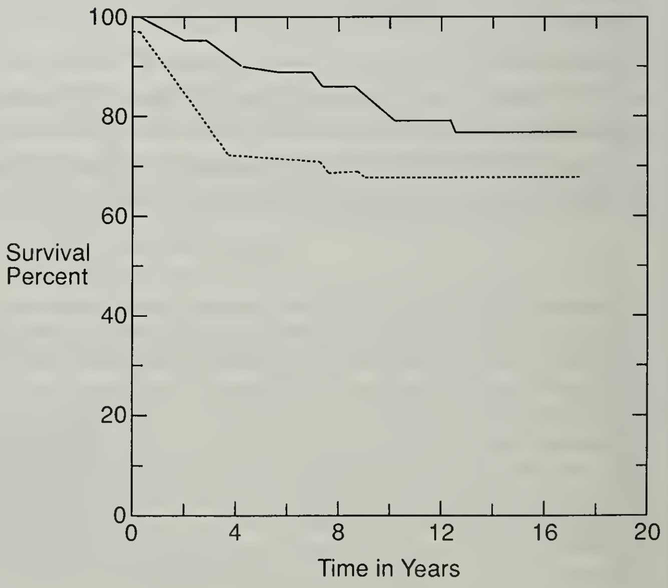

Figure 1
Actuarial survival (solid line) and freedom from relapse actuarial survival (dotted line) for 239 PS I & II Hodgkin's disease patients.

Table 2

Current Status of 239 PS I & II Hodgkin's Patients

Number of Patients	*Status*
167 (70%)	Alive: no relapse following initial therapy.
39 (16%)	Alive: relapsed following initial therapy-successfully salvaged.
9 (4%)	Died of non-Hodgkin's related cause. Initial therapy successful.
19 (8%)	Died of Hodgkin's disease.
5 (2%)	Died of non-Hodgkin's related cause. Relapsed following initial therapy-successfully salvaged.

the majority of the PS I and II patients. Patients were included in this review if they met the following criteria: 1) Biopsy confirmation of Hodgkin's disease; 2) A formal staging laparotomy with splenectomy; 3) PS IA, IB, IIA, or IIB disease confined to the supradiaphragmatic region.

Two hundred thirty-nine patients met the study criteria and the clinical features of this population including male to female ratio, age, stage, and pathologic subtype are summarized in Table 1. Twenty-six percent of the patient population had PS I and 74%.had PS II disease. Only 13% of the patients presented with "B" symptoms.

Initial treatment for all 239 patients is also summarized in Table 1. Total nodal radiation therapy generally consisted of mantle field treatment to a total dose of 4,000-4,400 cGy followed by treatment to the para-aortic region, splenic pedicle, and pelvis to a total dose of 3,600 cGy. Subtotal nodal radiation therapy was similar to total nodal treatment but with treatment to the pelvis omitted. As Table 1 indicates, 89% of the patients initially were treated with either total nodal or subtotal nodal radiation therapy: S(TNI). Involved field (IF) or extended field (EF) radiation therapy generally involved treatment to a limited field which encompassed either the site of initial presentation (IF) or the addition of the next adjacent chain of lymph nodes (EF) to a total dose of 4,000-4,400 cGy. Radiation therapy alone with either S(TNI) or IF/EF was the initial treatment for 94% of the PS I and II patients. A small fraction of the PS I and II patients (6%) also received combination chemotherapy in addition to radiation therapy as initial therapy. Indications for the addition of chemotherapy to RT included "B" symptoms, a poor response to radiation, or massive disease at presentation (ie, large mediastinal disease).[6]

Patients who suffered a relapse following initial therapy were treated with either combination chemotherapy alone or combined modality therapy with chemotherapy plus low dose radiation therapy.[6,13]

All patients were followed at regular intervals of three to six months. All recurrences were documented with biopsies. The follow-up time for the PS I and II patients varied from a minimum of one year to a maximum of 18 years with a mean follow-up time of 7.3 years. Survival curves and freedom from relapse (FFR) survival curves were generated using both the Kaplan-Meier technique and the life-table method.[14,15]

Results

Table 2 summarizes the outcome for all 239 PS I and II patients. Only 19 patients (8%) have ultimately died of Hodgkin's disease. This is due to two factors: 1) 176 patients (74%) went into complete remission following initial therapy and did not experience a relapse; and 2) 63 patients relapsed following initial therapy; however, subsequent salvage therapy was successful in 44 (70%) of these 63 patients.

Fourteen patients (6%) have died of non-Hodgkin's related causes in addition to the 19 patients (8%) who died of Hodgkin's disease. Therefore, 206 patients (86%) are alive with a mean follow-up of over seven years. Fig. 1 shows the actuarial survival and the freedom from relapse (FFR) actuarial survival curves for all 239 patients. The five-year and 10-year actuarial survival rates are 89.6% (± 4.2%, 95% confidence limits) and 80.8% (± 6.9%), respectively. The actuarial 18-year survival rate is 78%.

The FFR survival curve in Fig. 1 clearly demonstrates that the vast majority of relapses following initial therapy have occurred in the first four years following treatment. The probability of relapsing 10 years or more after initial therapy was extremely small.

Discussion

Three radiation therapy departments in Connecticut have consistently used (SL+RT) for early Hodgkin's disease and this strategy has produced excellent long-term results. The combination of successful initial therapy with 94% of the PS I and II patients treated with radiation therapy alone plus highly successful salvage therapy with chemotherapy for relapsing patients has resulted in only 19 of 239 PS I and II patients dying of Hodgkin's disease and an 18-year survival rate of 78%. Our data are completely consistent with the Stanford University results which demonstrate a 15-year survival rate of 79% using primary radiation therapy for 416 PS I and II Hodgkin's patients.[16]

It would be more convenient and somewhat less morbid if some CS I and II patients could avoid a SL. Some studies have defined subgroups of CS I and II patients who may not require a SL because of the low probability (less than 10%) that the SL will be positive.[1] These subgroups may include females with CS IA disease and males with CS IA disease and either a high neck presentation or lymphocyte-predominant pathology.[1] Therefore, it may be reasonable to forgo the SL in some selected cases. However, in our study, only 24% of our patients had PS IA disease. Therefore, even if one applies the criteria of selectively avoiding SL for some CS IA patients, the vast majority of patients will still require a SL. In addition, the SL allows for much more precise radiation treatment planning and smaller fields below the diaphragm thus reducing the radiation dose to many critical structures such as the small bowel, kidneys, and ovaries.

As we move into the 1990s, it is clear that a variety of innovative treatment options will be developed for early stage Hodgkin's disease. These options may include: 1) Initial therapy with less toxic chemotherapy for CS I and II patients without the necessity of SL; 2) A combination of involved or local field radiation plus chemotherapy without SL; 3) Radiation therapy without SL with chemotherapy for salvage. However, several issues must be clearly defined before embarking on any of these newer strategies. First, it is highly unlikely that any alternative to (SL+RT) will produce a higher cure rate. Second, newer strategies should be considered only if they can reduce the overall morbidity compared to (SL+RT). Since these alternate options will all result in a higher fraction of Hodgkin's patients receiving chemotherapy, there must be substantial and convincing long-term evidence that the newer chemotherapy regimens are safer than radiation therapy alone. Finally, it will take 10-20 years of close follow-up to actually demonstrate the superiority, equivalence, or inferiority of any new treatment programs.

Based on the long-term successful results of this study, we strongly recommend that (SL+RT) remain one of the main treatment strategies of early Hodgkin's disease. The use of this approach will clearly be modified over time. However, all patients with early Hodgkin's disease should be informed of the excellent long-term results of (SL+RT) in curing Hodgkin's disease. Because of the consistent success of (SL+RT), treatment strategies other than (SL+RT) should be tested in carefully designed prospective clinical trials.

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Obstructing Cancers of the Right and Left Colon: Critical Analysis of Perioperative Risk Factors, Morbidity, and Mortality

SUBHAJIT DATTA, M.D. AND JOHN P. WELCH, M.D.

ABSTRACT—Significant hospital mortality has been observed in right-sided obstructing colonic cancer patients but remains unexplained. The medical records of 52 patients with obstructing colonic cancer seen between 1980-88 were reviewed to identify prognostic factors influencing mortality when carcinoma involved either the right or the left segments of the colon. The mean age, sex, incidence, and distribution of perioperative risk factors and rate of postoperative complications were comparable between the two groups.

Right colonic cancer patients had a higher incidence of advanced disease (16 of 19 had Dukes C and D tumors). Their mortality was higher than that of their counterparts (21% vs 9%), correlating primarily with advanced cancer stage rather than with preoperative risk factors or technical (operative) complications. Though the difference in mortality rates is not statistically significant, patients with obstructing cancers of the right colon, compared to their left counterparts, are hospitalized in more advanced stages of disease and have a worse prognosis.

EXCLUDING skin cancer, colon cancer remains the second most common malignant lesion in the United States.[1,2] The incidence among both males and females varies regionally and is consistently high in Connecticut. In the last 25 years there has been little improvement in the survival of patients with this form of cancer.[3] While the perioperative mortality associated with these lesions ranges from 3-9%,[3-5] it is as high as 15-30% when obstruction is present.[3,4] Of further interest, some studies suggest that obstructing right colonic cancers may be associated with higher mortality rates than their left counterparts.[3,6]

Materials and Methods

The medical records of all patients with acutely obstructing colon cancer hospitalized at Hartford Hospital from 1980 to 1988 were reviewed. During this period, a total of 1,622 patients were admitted to the hospital (45.9% had right-sided lesions: 25.4%, cecum; 15.2%, ascending colon; and 5.3%, hepatic flexure; and 54.1% had left-sided lesions: 4.7%, left transverse colon; 5.3%, splenic flexure; 8.2%, descending colon; and 35.9%, sigmoid colon). Cancers involving the cecum, ascending colon, hepatic flexure, and right half of the transverse colon were labeled right colonic cancers (RCC), while those in the left half of the transverse colon, splenic flexure, descending colon, and sigmoid were grouped together as left colonic cancers (LCC). Anorectal cancers were excluded from this study. "Perioperative period" was defined as either the entire duration of the same hospitalization (until discharge) or a duration of one month following the operative date during a long hospitalization. Age, sex, presence of other medical diseases including operative risk, a modified Dukes staging system,[7,8] and histologic grades were critically reviewed in search for any correlation with the mortality and morbidity. Finally, the mortality and morbidity, as well as possible predisposing factors found in patients with obstructing right and left colonic cancer, were compared. The duration of symptoms was inadequately recorded and hence was not considered in this study. Patients with either small bowel obstruction due to metastatic disease or intestinal perforation associated with obstruction were also excluded from analysis.

Results

A total of 52 patients with obstructing colonic cancer were found among all admissions from 1980-88. Of these, 33 originated in the left colon, while 19 were situated in the right colon.

The age of patients with LCC ranged from 53-90 (mean 73 years), while the age of the remaining patients was from 52-82 (mean 72 years).

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Table 1

Preoperative Medical Risk Factors

	Obstructing L Colon Cancer	Obstructing R Colon Cancer
Cardiovascular	19	10
Respiratory	4	1
Gastrointestinal	3	2
Renal	2	0
Liver	1	0
Neurologic	2	0
Other CA	3	0
Metabolic/Nutr.*/Other	10	4
Total	44	17

*Nutritional

Nine of 19 RCC patients were females, whereas 10 were males (52%). Twenty-two of 33 (66%) LCC patients were females and 11 (33%) were males. All four deaths among RCC patients were in females and two of three LCC deaths were in females.

Operative risk factors were analyzed. There were 44 significant medical risk factors in 33 LCC patients, averaging 1.33 per patient. These included symptomatic atherosclerotic heart disease including angina pectoris, previous myocardial infarction, congestive cardiac failure, supraventricular and ventricular arrhythmias, and hypertension; peripheral vascular disease; chronic obstructive pulmonary disease secondary to prolonged smoking or asthma; peptic ulcer disease; a history of cerebrovascular disease including transient ischemic attacks; parkinsonism; gout; nutritional depletion including patients with anemia and a history of carcinoma (prostate, kidney, and breast in three separate patients) (Table 1).

Nineteen RCC patients had a total of 17 significant medical risk factors averaging 0.9 per patient. These included symptomatic atherosclerotic heart disease, partial heart block, supraventricular and ventricular arrhythmias, hypertension, chronic obstructive pulmonary disease, postgastrectomy malnutrition and anemia, and diabetes mellitus (Table 1).

Table 2

Pathologic Staging

	Right Colonic Cancers	Left Colonic Cancers
A	0	0
B1	0	1
B2	3	15
B3	0	1
C1	0	1
C2	6	9
C3	1	1
D	9	5

Disease stage was analyzed according to a modified Dukes classification (Table 2).[7,8] Two of the Dukes D RCC patients had unresectable, fixed cancers, as did one of the Dukes D LCC patients. Of the three deaths in LCC patients, two had Dukes B2 tumors and another had a Dukes D lesion. Among the four deaths in RCC patients, two patients had D tumors, one a C2 lesion, and one a C3 tumor.

The histologic grading is reviewed in Table 3. Of the three LCC patients who died, two had moderately differentiated cancers, while one had a poorly differentiated cancer. There were four deaths among RCC patients; two had moderately differentiated cancers and two had poorly differentiated ones.

Table 3

Histologic Grading

	Left Colonic Cancers	Right Colonic Cancers
Well differentiated	4	0
Mod. differentiated	24	15
Poorly differentiated	5	4

The operative procedures performed on these patients are summarized in Table 4. Seventeen of 33 LCC patients (52%) had uncomplicated postoperative courses. The remaining 16 individuals (48%) had a total of 32 complications and three deaths. Nine of 19 (47%) RCC patients had uncomplicated hospitalizations, whereas the remaining 10 had 20 complications, and four of them succumbed.

Perioperative complications encountered in these patients are shown in Table 5. Technical surgical complications are summarized in Table 6. In Table 7, a comparison of perioperative complications and preoperative risk factors is made. The average duration of hospitalization for LCC patients was 27 days (range 11-60 days) while it was 19 days for RCC patients (range 12-29 days). Comparable patients had a longer hospital stay in the first half of the decade when compared with patients in the last half. Prolonged hospitalizations in several patients with multiple complications influenced the statistics as well.

Three of 33 (9%) LCC patients died during the perioperative period, while four of 19 (21%) obstructing RCC patients succumbed (Table 8). Though these data

Table 4

Operative Procedures

		Number
Right Colon	Right hemicolectomy & anastomosis	16
	Ileotransverse colostomy (palliative)	3
Left Colon	Tube cecostomy, later resection & anastomosis	11
	Loop transverse colostomy, later resection & anastomosis	10
	Cecostomy with resection & anastomosis	2
	Colostomy with resection & anastomosis	2
	Hartmann procedure	6
	Resection, colostomy & mucous fistula	2

show a higher perioperative mortality for obstructing RCC, statistical analysis χ^2 revealed no significance (P=0.2); this was mainly due to the small number of patients. No correlation was found between the operative procedures and subsequent mortality and morbidity.

The three deaths with LCC were in patients with significant operative risks (Table 9). One patient with known cirrhosis and chronic renal failure died of cardiorespiratory and renal failure following a Hartmann procedure. A female with advanced cardiovascular and cerebrovascular disease died following a cerebrovascular accident with cardiac failure and pneumonia. The third patient had a history of emphysema and died as a result of pneumonia and respiratory failure.

Four patients with obstructing RCC died in the perioperative period. Three of these deaths could be attributed to advanced stages of disease rather then preexisting medical illnesses. A 92-year-old female without known cardiac disease succumbed with cardiorespiratory complications and ascites following a right hemicolectomy. Another patient with extensive liver metastases died of multisystem failure and nutritional depletion after a right hemicolectomy. A 51-year-old female with Dukes C2 tumor and malnutrition who died following a massive myocardial infact had no history of cardiac disease. The final death may have followed an anastomotic leak or infection of malignant ascites; death was preceded by an ascitic leak, wound dehiscence, and a prolonged period of ileus.

Table 5

Perioperative Complications

	Obstructing Left Colon Cancer	*Obstructing Right Colon Cancer*
Cardiovascular	5 (16%)	6 (30%)
Respiratory	5 (16%)	3 (15%)
Gastrointestinal	9 (28%)	4 (20%)
Urologic	8 (25%)	1 (5%)
Liver	0	1 (5%)
Meta*/Nutr+/Others	3 (9%)	5 (25%)
Neurologic	2 (6%)	0
Total	32	20

*Metabolic
+Nutritional

Discussion

It has been observed that obstructing colonic cancer poses a higher perioperative risk to the patient than elective surgery for colonic cancer.[3-6,9,10] Efforts are being made to identify the prognostic indicators related to colonic cancer in order to formulate better treatment policies.[4-6,11] Some investigators have reported that tumor location is an important prognostic factor, and excluding rectal and rectosigmoid cancers, obstructing RCC patients have a worse prognosis than their left-sided counterparts (prospective study),[6] though conflicting reports can be found.[11] The present study compares the perioperative mortality and morbidity of right and left colonic cancer patients without analyzing the long-term survival.

Table 6

Technical Complications of Operations

		Number
Right Colon	Subhepatic abscess	1
	Fascial dehiscence, ? anastomotic leak	1
Left Colon	Rectal bleeding, ? suture line	1
	Cecostomy leak-peritonitis	1

Approximately 125 patients undergo colonic surgery for colonic cancer every year at Hartford Hospital; 5.5 % of this group present with large bowel obstruction due to malignant lesion itself. As expected, a higher number of patients with complete large bowel obstruction had LCC than RCC. In the clinical trial of the National Surgical Adjuvant Breast and Bowel Project (NSABP), it was noted that obstruction was more likely to occur in the descending colon, especially at the splenic flexure.[5]

Though not statistically significant (P=0.2), obstructed RCC patients had a higher hospital mortality (21%) when compared to LCC patients (9%). This fact has been noted by others,[7] but controversy exists as to the cause of this variance. Efforts to unravel this question was the primary goal of this study. Of interest, the incidence of perioperative complications involving other organs was similar between the two groups (48.5% VS 47.4%).

The magnitude of the *initial* operations were, in most cases, more major for right-sided cancers than for left-

Table 7

Relationship Between Past Medical History and Mortality and Morbidity

	Total patients	*Total patients with morbidity*	*Morbidity related to PMH**	*Morbidity unrelated to PMH*
L Colonic CA	33	16	8	8
R Colonic CA	19	10	1	9

*Past Medical History

sided ones. A right colectomy with anastomosis usually requires between two and three hours to perform compared to approximately one hour for a loop transverse colostomy or tube cecostomy. Since the patients were obstructed at the time of these operations, the risk of morbidity and mortality was, indeed, higher. On the other hand, four of the patients with cancers of the left colon had anastomoses at the first operation and 21 others had later resection and anastomoses, all of which were major operations. The 21 patients who had delayed resection and anastomoses had the theoretical advantage of decompression, medical stabilization, etc. prior to surgery.

No difference in age was found between the two groups and there was a predominance of female patients, especially in the LCC group. Six of the seven deaths occurred in females. The significance of this is unclear, considering the small group of patients. Though the incidence of colon cancer among females may be increasing, the mortality has tended to be lower than that in the male population.[1]

Finally, attention was focused on the preoperative risk factors, disease staging, and the histologic grading. The relationship between preoperative risk factors and perioperative morbidity is shown in Table 5, but fails to show any particular trend. Medical risk factors contributed in three deaths in LCC patients. On the other hand, among patients who succumbed with RCC, analysis failed to implicate any preoperative medical risk factors other than disease stage which would explain their outcome.

A significant number of patients in both groups had advanced stages of disease (16), but this was more prominent in the right colon cancer group (Stage D—nine patients, Stage C3—one patient, Dukes C2—six patients, out of a total of 19 patients). Mortality among RCC patients was associated with Dukes D staging in two, Dukes C3 in one, and Dukes C2 in one. On the other hand, in the LCC group, two of the three deaths occurred in patients with Dukes B2 tumors and in one with a Dukes D tumor.

No significant relationship was found between histologic grade and perioperative mortality and morbidity for obstructed right and left colon cancer patients.

Though the number of patients studied is too small to establish any statistically significant relationship, the data suggest that patients with right colonic obstruction present at a later stage of their disease. All four deaths in the RCC group occurred in patients with advanced disease. Characteristically, right colonic (especially cecal) tumors are large by the time obstruction develops. Several authors have reported that advanced disease is responsible for the poor prognosis in obstructed cancer patients.[5,7,12] On the other hand, tumor size in itself has been shown to be of no prognostic significance.[13,14] It has also been emphasized in a report that this discrepancy in mortality among patients with obstructed RCC is unrelated to tumor encirclement and nodal status, although the study excluded Dukes D tumors (which form a large proportion of our study group).[6] Hence, we conclude that right colonic obstruction is associated with more advanced stage tumor which may be responsible for a high perioperative mortality. The potential risk of anastomotic leaks in this population should also be kept in mind, especially in the presence of factors such as ascites, hypoalbuminemia, and liver metastases. Further studies with larger groups of patients will be necessary to elaborate upon this question.

Table 8

Mortality Rates

	Obstructing Left Colonic Cancer	*Obstructing Right Colonic Cancer*	*Total*
Total # patients	33	19	52
Deaths	3 (9.1)%	4 (21.1%)	7 (13.5%)

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Table 9

Analysis of Deaths

	Age/Sex	*Clinical Presentation*	*Preoperative Risk Factors/PMH*	*Lesion*	*Procedure*	*Postoperative Complications*
Right colon cancer	81/F	Weight loss, constipation, vomiting, distention	Hypertension, ascites	Cecum, Dukes D, unresectable	Ileotransverse colostomy	Ascitic leak, prolonged ileus, malnutrition, multisystem failure
	75/F	Constipation, pain, destention	None known	Cecum, Dukes D, liver metastasis	R hemicolectomy	Liver failure, multisystem failure
	51/F	Pain, distention, vomiting	None known	Cecum, Dukes C2	R hemicolectomy	Malnutrition, myocardial infarction
	92/F	Pain, distention, constipation	Anemia	R transverse colon, Dukes C3	R hemicolectomy	Prolonged ileus, ascites, ventilator dependent
Left colon cancer	72/M	Pain, obstipation	COPD, chronic renal failure, cirrhosis,CHF, metastatic prostatic CA	Dukes B2	Hartmann procedure	Prolonged ileus, acute renal failure, respiratory arrest
	79/F	Pain, distention constipation	ASHD, previous CVA, MI, diabetes mellitus	Dukes B2, splenic flexure	Cecostomy, L hemicolectomy	Cardiorespiratory failure, acute renal failure, ischemic encephalopathy
	94/M	Distention, pain, constipation	ASHD, emphysema	Dukes D, sigmoid colon	Transverse colostomy	Pneumonia

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Important Advances in Clinical Medicine

Plastic Surgery

The Scientific Board of the California Medical Association presents the following inventory of items of progress in plastic surgery. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, or scholars to stay abreast of these items of progress in plastic surgery that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Plastic Surgery of the California Medical Association, and the summaries were prepared under its direction.

Lymphedema

LYMPHEDEMA is incurable despite intensive surgical and medical efforts. Its cause is unknown. Significant swelling develops in about 1% of patients after axillary or inguinal node dissection, but not in the other 99%. A congenital predisposition may underlie the development of lymphedema.

Most patients are best treated by conservative measures, especially elastic compression stockings, weight loss, and the judicious use of diuretics.

Surgical treatment is used when enlargement of an extremity causes functional impairment. Relatively modest increases in the circumference of an extremity can represent liters of fluid, thus causing the patient to carry several kilograms of extra weight. In addition, recurrent cellulitis can be a difficult and disabling problem. These problems can be ameliorated substantially by surgical intervention.

The surgical treatment of lymphedema is divided into two approaches: physiologic (attempts to reconstruct lymphatic flow) and excisional (the removal of varying amounts of skin and subcutaneous tissue). Encouraging results with the use of lymphatic grafts, lymphatic anastomoses, and lymphatic-venous anastomoses have recently been reported. Although improvement is seen, cure is still not possible. Other operations such as the buried dermal flap and omental transposition have been generally discarded in favor of more successful approaches.

The operative procedure that provides the most consistent improvement of lymphedema with the lowest incidence of complications is extensive skin and subcutaneous excision beneath skin flaps. In a series of more than 100 patients treated by this method, about 70% have notable clinical improvement with a reduction of extremity girth of more than 50%. The more skin and subcutaneous tissue removed, the better the postoperative result.

In the future we should see improved microvascular procedures to reconstruct lymphatic flow. The key to more successful surgical approaches is likely to be earlier intervention before swelling is well established, fibrosis results, and the permanent destruction of lymphatics and their delicate valvular mechanisms occurs.

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Early Reconstruction of Facial Burns

MOST facial burns are appropriately treated with local wound care and topical antibacterials and heal promptly with minimal scarring. When treated in this way, however, 5% to 10% fail to heal or do so with considerable scarring. In this instance, late reconstruction is required.

Early excision and grafting has become the standard method of treating deep burns of the nonfacial areas of the body but has not been used on deep facial burns until recently. Instead, routine, thin skin grafts were placed on granulation tissue, planning on late reconstruction. The technique of early excision and grafting shortens the hospital stay; using aesthetic units rather than small patchwork grafts improves appearance.

Obvious third-degree face burns are prepared for excision and grafting. Indeterminate face burns are treated with twice-a-day hydrotherapy and topical antibacterials for ten days. At that time the patient's face is evaluated and those aesthetic units that are judged unlikely to be healed by three weeks are scheduled for excision and grafting. The facial units are excised and porcine xenograft applied. A day or two later, the patient is returned to the operating room and a negative impression is taken over the xenograft. Thick, split-thickness grafts from the blush area are then harvested at 0.046 to 0.061 cm (0.018 to 0.024 in) in adults and proportionately thinner in children. These are carefully stitched into place and dressed with compression dressings. The dressings are removed twice a day and the grafts examined for slippage or hematomas. Pressure devices are worn until the grafts are mature.

Patients treated in this way frequently require revision of the mobile areas of the face. But the revisions are minor procedures and well tolerated by the patient and family. The large facial blocks, such as forehead and cheeks, do not require late reconstruction.

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Breast Implants and Cancer Detection

THE modern silicone breast implant was first introduced in 1963, and since then well over two million women in the United States (one in 33 between the ages of 20 and 60) have had their breasts enlarged or reconstructed using this device. Uncounted more have received silicone injections for the same purpose—a procedure that has fortunately fallen into disrepute. As the median age for implantation is 32, a substantial number of women are approaching, or are well into, the cancer risk age group, thus representing a significant public health issue.

Table 1

Breast Cancer Stage Distribution

Cancer Type	*All Patients in Los Angeles County, %*	*Implant Patients in Los Angeles County, %*
In situ	7.1	12.5
Local	50.2	50.0
Nonlocal	42.7	37.5

Self-detection and physical examination do not seem to be influenced by the presence of an implant. Because the silicone is radiopaque, however, mammography reliability can be diminished. Breast tissue can be hidden by the implant or compressed to a density that obscures subtle lesions.

New technology is now available by which the breast can be pulled or pinched in front of the implant, substantially improving the quality of the image and the amount of tissue viewed. This, combined with extra tangential views of obscured areas, can produce high-quality, diagnostically reliable mammograms. If a firm capsular contracture is present, this technique may not be as effective.

Are women who have had breast augmentation at risk for a delayed detection of cancer? Certainly they are theoretically at risk, and every woman should be so advised. Thus far, however, there have been no substantiated reports in the medical literature of any woman whose cancer detection was delayed because of an inability to recognize early tumors by mammography. In a study of 3,111 Los Angeles women, no delay in the detection of cancer, even with pre-"pinch" technology mammography, was found. Thus the risk, while real, would appear to be slight. The table compares these patients with all age-matched Los Angeles women without augmentation.

The American Society of Plastic Surgeons and the Society of Breast Imaging have recommended the following cancer screening program:

- *Examination*. Follow the American Cancer Society recommendations for monthly self-inspection. Annual physical examinations by physicians with experience in examining augmented breasts should be routine.
- *Mammography*. Preoperative mammograms should be obtained for women older than 35 years, every one to two years for women aged 40 to 50, and annually thereafter. High-volume screening clinics in which two quick

views are taken should not be used. Mammograpy should be done in the same center each year by qualified mammographers who will make an effort to tailor the test to each woman. While these diagnostic studies are more expensive, the low-cost screens can be unreliable and therefore worthless.

Women who have had silicone injections become impossible to examine because the silicone often forms multiple granulomatous masses, and mammograms are unreadable. These women have given up forever the ability to detect carcinoma before it has spread beyond the breast. Subcutaneous mastectomy and reconstruction should be seriously considered in this population.

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Melanoma Update

MALIGNANT melanoma should no longer be considered rare. With sunlight exposure as a proven etiologic factor, its rate of increase is exceeded only by that of bronchogenic carcinoma. The median age continues to be younger than 50 years and, like other neoplastic disease, melanoma is curable if detected at an early stage.

The most effective treatment of the early stages of melanoma continues to be surgical extirpation. It plays a primary role in the management of patients with stage I disease (primary melanoma) and stage II disease (recurrence of tumor in the local regional area) and a limited role in the treatment of stage III (distant metastases). Thin (<1 mm) lesions can be cured with narrow margins (1 cm), whereas thicker lesions require 2- to 5-cm margins to decrease the risk of local recurrence. Solitary metastases to the brain, subcutaneous areas, or even lymph nodes may be suited for extirpation with a reasonably good prognosis.

The role of lymph node dissection is controversial, although data suggest a prolonged survivorship in patients with intermediate-thickness (1.5 to 4 mm) melanoma who undergo such operations. Surgical extirpation is also important in the palliation of extranodal extension to prevent the breakdown of overlying skin and soft tissues. Radiation therapy continues to be mainly palliative, especially with bony metastases.

Dacarbazine (DTIC) has been the most extensively used chemotherapeutic agent. When used as a single agent, this mode of therapy can produce response rates of 15% to 20%, largely in controlling soft tissue disease. Complete remissions are few (less than 5%) in most series.

Biologic therapy with interferon has produced responses in as high as 22% of patients with disseminated malignant melanoma. Interleukin 2 and lymphokine-activated killer cells have also been effective: Response rates with this combination have been 20% to 30%. Treatment recommendations, therefore, include wide surgical extirpation for thick melanomas, selective regional adenectomy, and systemic therapy in some patients.

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Lower Extremity Reconstruction

LOWER extremity reconstructive goals following severe trauma include restoring limb function, covering vital structures, and maintaining a satisfactory appearance. Techniques available to meet these goals include fasciocutaneous flaps, muscle flaps, tissue expansion, and free tissue transfer. Several new procedures have been introduced that expand treatment alternatives and permit the successful management of lower extremity soft tissue and bone defects.

Deficits involving skin and subcutaneous tissue are amenable to treatment using skin grafts, pedicle flaps with or without a defined vascular supply, and fasciocutaneous flaps. The lateral supramalleolar flap has been described recently and offers stable soft tissue coverage of the lateral malleolus. Fasciocutaneous flaps have shown their usefulness in the soft tissue reconstruction of the distal lower leg. Finally, V-Y flaps of skin and fascia based on perforating vessels entering the flap from its deep surface have been used to cover metatarsal heads, the posterior heel, and the lateral malleolus. These V-Y flaps appear reliable and are versatile in design.

Muscle and musculocutaneous flaps continue to demonstrate their versatility. The biceps femoris musculocutaneous flap has been shown to have an extended application in lesions of the anterolateral thigh. The medial gastrocnemius muscle is being used with increasing frequency to cover a threatened or exposed knee prosthesis. In addition, muscle transferred into a fibrotic cavity has been shown to increase the antibiotic concentration in that area.

Tissue expansion in the lower leg offers promise for difficult scar reconstructions but has a higher complication rate than in other areas because of problems with skin instability and the constricting deep fascial layer. When appropriate precautions are taken, however, tissue expansion for lesions below the knee can be done successfully. This involves the use of a temporary silastic bag injected with an increasing volume of a saline solution.

A recent innovation has had an effect on orthopedic and plastic surgery. After a careful corticotomy is done, bone can be slowly separated using an external fixator, with the regeneration of new bone at the osteotomy site. This permits the lengthening of bone along with the correction of angulation and rotational deformities. This technique may prove useful in the treatment of the bony deficit in osteomyelitis. The area of bone infection could be excised and the proximal bone lengthened to bridge the deficit.

Free tissue transfer using microsurgical techniques continues to expand the lower extremity reconstructive horizons. The application of the insensate scapular free flap with its thin, well-vascularized skin paddle has recently been described for the treatment of foot wounds. If this skin is carefully tailored and the excess trimmed, it is possible to achieve foot reconstruction on the plantar surface. It is now known that the fibula transferred as a vascularized graft can be osteotomized and folded on itself to provide a strong reconstruction for the tibia. A recent series reinforces the concept that osteomyelitis can be successfully managed by bone debridement, free muscle transfer, and delayed bone grafting. Free tissue transfer techniques are being applied to patients with severe peripheral vascular disease in whom the only alternative is amputation.

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Facial Reanimation

RESTORING normal facial movement after facial nerve damage is challenging. Spontaneous animation and the creation of a normal balanced smile can only be accomplished by reinnervating the paralyzed facial muscles with facial nerve fibers from the ipsilateral side. Therefore, in cases of distal seventh nerve injuries, interpositional nerve graft reconstruction is the most physiologic approach. If facial paralysis is due to intracranial injury, however, other more complicated forms of reconstruction are necessary.

Nerves from the ipsilateral side of the face can be transferred to the distal facial nerve to reinnervate the muscles. These include the hypoglossal, lingual, phrenic, greater auricular, spinal accessory, and the ansa-cervicalis. Portions of the temporalis, masseteric, and frontalis muscles can be transferred to mimic facial muscle movement. Muscle contractions after such techniques are not spontaneous, and a synthetic smile must be learned and practiced.

With the introduction of microvascular surgery, techniques have been devised to create more spontaneous facial muscle activity. A cross-facial nerve graft and a functional muscle transplantation are used in a two-stage operation to reanimate the face. During the first stage, a sural nerve graft is connected to distal branches of marginal mandibular, buccal, or zygomatic branches of the unparalyzed facial nerve. This nerve graft is tunneled subcutaneously below the lip. The free end of the nerve graft is left subcutaneous near the tragus on the paralyzed side.

Over the next six to eight months, the axons from the unparalyzed side grow across the sural nerve graft to the paralyzed side. The axonal growth can be followed by percussing over the nerve graft until an electrical shock sensation is elicited.

Once Tinel's sign is detected on the paralyzed portion of the face, the second-stage operation is done. A frozen-section biopsy of the free end of the cross-facial nerve graft is done to determine if axons have in fact grown from the unparalyzed side to the paralyzed side. If axons are present on frozen section, then the serratus anterior muscle is transplanted from the back to the face. The artery and vein to the serratus anterior are microsurgically anastomosed to the facial artery and vein. The free end of the sural nerve graft is repaired to the long thoracic nerve of the serratus anterior muscle.

The nerve will eventually grow into the newly transplanted muscle and functionally innervate the muscle. Eventually, when the patient moves the unparalyzed side of the face, nerve impulses will travel across the nerve graft and stimulate the transplanted serratus anterior muscle. This approach can restore some spontaneous animation, particularly in patients younger then 50.

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Soft Tissue Augmentation

IDENTIFYING a safe, lasting substance for use in soft tissue augmentation continues to challenge plastic surgeons and dermatologists. The most widely accepted substrate for such use is Zyderm collagen implant, approved by the Food and Drug Administration (FDA) in 1981. It is composed of enzymatically purified bovine collagen suspended in a saline solution and comes in two concentrations, Zyderm I and II. Both are recommended for the diminution of facial wrinkles, acne scars, and other depressed scars. Neither is recommended for larger defects. Correction is transient, and touch-ups are necessary every 4 to 12 months to maintain correction. Zyplast, collagen cross-linked by glutaraldehyde, was introduced in 1985. The cross-linking stabilizes the collagen against degradation but not to the extent initially hoped. Touch-ups are required on a 4- to 24-month basis. The use of Zyplast is recommended for the correction of deeper contour deficiencies. Pretreatment skin tests to determine hypersensitivity are necessary. It is now recommended the skin test be repeated at four weeks to decrease the incidence of treatment-associated hypersensitivity reactions.

There has been a continual interest in autologous fat grafting since its first use in 1893. Doubts linger as to the stability of correction beyond three to four months, and many still doubt the efficacy of this technique. Small fat grafts (4 to 6 mm in diameter) have been injected in a manner similar to the use of collagen with variable results. Supporters of the technique argue that correction lasts longer and sensitivity reactions are less severe. All agree that resorption will occur, and overcorrection and touch-ups are necessary. Inflammatory reactions, firmness, and lumpiness have been reported. In the laboratory, an adipocyte precursor with the potential to differentiate into mature adipocytes has been identified. Single-cell suspensions of these cells may show promise in creating true fat pads where injected.

Fibrel gelatin matrix implant has been approved by the FDA for the treatment of depressed scars. Reports claim an average loss of correction by 20% at two years. Local reactions have been mild, and no other adverse reactions have yet been reported. Medical grade silicone (polydimethylsiloxane) is not commercially available but continues to be used by a few practitioners. When used, proper technique is essential; there is no room for error. Technique-related problems and severe local reactions to the silicone have been reported.

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Maxillofacial Trauma

THE diagnosis, management, and treatment of complex craniomaxillofacial trauma are challenging for plastic and reconstructive surgeons. Maxillofacial trauma is usually considered a phenomenon of youth, but current population trends indicate the average age is increasing. There is a 50% longer median hospital stay in patients older than 65 compared with younger groups. This increased time is due to multisystem injuries, rather than the extent of maxillofacial fracture. Periodontal disease, bone resorption, and dental restorations or missing teeth are much more frequent in the geriatric age group. Rigid internal miniplate fixation eliminates some of the problems of intermaxillary wire fixation, resulting in fewer complications—that is, less risk to crown or bridge work, less weight loss, and decreased breathing problems.

The timing and staging of craniofacial fractures repair have traditionally been weighed against other possible life-threatening conditions. The early repair of facial fractures does not appear to affect adversely the recovery or outcome in patients with head injuries, however.

Much attention has recently been focused on rigid fixation (miniplates) as a method of improving fracture healing. It has been shown that fixation by means of interfragmental stabilization and compression tends to neutralize torsional and sheer forces, allowing primary bone healing and union. Rigid fixation is therefore indicated in cases where onlay bone grafts may be exposed to motion, shear, and torsional forces.

Recent contributions clearly substantiate the basic principles of maxillofacial treatment: accurate diagnosis, early anatomic fracture reduction, stable osseous fixation, and the restoration of preinjury occlusion. The care of older patients will continue to be challenging.

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Feeding Children Who Have Cleft Lip or Palate

SURGEONS have assumed that special feeding precautions should be adopted for children born with a cleft lip or palate or after the repair of these anomalies. Mothers in developing nations, however, consistently prove that immediate breastfeeding is safe.

Plastic surgeons should consider advising the use of breast or conventional bottle and nipple combinations. Most children with clefts, even those with enormous tissue gaps, will do well at breast or bottle. Only a few will require special attention or special devices. Those few will require intensive and continuing attention because nutritional deficits impair future learning capacity.

What about feeding policy immediately after surgical repair? Comparative studies show no greater rate of complication if an infant is returned immediately to mother's breasts after lip repair. There is no evidence that a short, soft nipple or a carefully directed tip of a spoon will cause palatal dehiscence.

Perhaps the greatest mechanical hazard after lip or palate procedure, especially the latter, is a child's finger directed into the mouth. Elbow restraints are therefore critical for a week after lip repair and two weeks after palatal repair.

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Quality Assurance—How Did We Come To This?

JOHN C. RUSSELL, M.D.

IN reviewing old office files, I recently found a monograph written by my predecessor, and former president of this society, Dr. Gerald O. Strauch, entitled "Quality Assurance—Buzzword or Signal of Progress."* Presented several years ago to our hospital's Board of Corporators, this was a thoughtful review of the history and current status of Quality Assurance. Would quality assurance help to contain costs by increasing efficiency while maintaining, and we would hope, improving the quality of patient care? Dr. Strauch was cautiously optimistic in his prediction: "I believe the answer to both questions is 'yes,' and I certainly hope I am right."

Contrast this prediction to a more recent and somewhat more jaundiced assessment of Quality Assurance by Bernard Jaffe, chairman of surgery at Downstate: "...Quality Assurance, despite its very positive attitude, is a flawed system. It is expensive, divisive, misdirected, and discriminatory. We may have to learn to live with its problems, but only if objective assessment documents that it is the best mechanism to accomplish the peer-review goal."[1]

Many of us involved on a daily basis with the bureaucracy known as *Quality Assurance* would agree. However well intentioned, Quality Assurance has gone far astray. Real quality problems exist, but Quality Assurance rarely gives us the necessary tools for their solution.

Quality Assurance (QA), a variant of the quality-control process familiar to industry, may function well in nonclinical areas. It functions poorly in evaluating physician performance.

As noted by Dr. Jaffe, physicians are commonly discriminated against in two ways. First QA may not "equally challenge the hospital's role in poor patient outcomes." Second, QA often assumes that the physician is "guilty until proven innocent." Until a physician is fully exonerated, often by litigation, "the paper trail attests to his/her culpability." Despite assurances of confidentiality and immunity, indiscriminant access to such information can occur, with possible disastrous consequences to the individual practitioner.

How did we come to this? I submit that Quality Assurance, the Malpractice Crisis, the National Practitioner Data Bank, the Resource Based Relative Value Scale, and the increasingly intrusive behavior of federal and private insurance programs that pay our fees, are at least, in part, simply different manifestations of the same public concern. They are poorly-focused reflections of the public perception of major deficits in the quality of medical care. Are we in any way to blame?

Evaluating the quality of physician performance raises many troubling questions. Are there problem physicians? What are their characteristics? How do we identify them? What has been our professional response towards the remediation or sanctioning of these physicians? If, as I think the public believes, we have failed in policing our own—why? Can we do better? Is QA the answer?

As we know, there is a poor correlation between medical "maloccurrences" and malpractice actions,[2] which suggests that other factors must play a role in the decision of a patient (or patient's family) to initiate malpractice proceedings. As we also know, malpractice suits are *not* randomly distributed. Less than 0.5% of practitioners generate approximately 30% of malpractice claims.[3] Some of this maldistribution can be attributed to the specialty distribution of physicians, and the relative risk of malpractice claims for each specialty: high for anesthesiology and surgical specialties, low for family practice, etc. However, both we and the public know that there *are* bad apples. Their behavior, often heralded in the media in spectacular fashion, demean our profession and each of us as individual physicians.

Among physicians, as among other professionals, there is a spectrum of knowledge, talent, competence, and, regretfully, ethics. Why has the public response to our imperfection been so severe? As a society, America in the 1990s is more cynical. It is unlikely that medicine will

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once gain rise onto the pedestal of paternalistic infallibility that we wistfully believe it once occupied. But investigative reporting which brings to light individual human frailties is an insufficient explanation for current societal distrust of medicine. I believe that it is the public's perception that despite our awareness of professional misconduct we, as a profession, have usually chosen not to act; this attitude of benign neglect has thrown open the door to public intervention and retribution. The Hippocratic Oath and the Oath of the American College of Surgeons are noble sentiments, but our actions, not our words, will be the final determinants of public perception and government action.

Who are the "problem physicians?" A potpourri of issues come to mind—substance abuse, physical or psychological infirmity, technical incompetence, inadequate or out-dated medical knowledge. The experience with "problem" medical students and residents identify those behaviors which are most difficult to correct. If unrecognized, or not effectively dealt with during medical school or residency training, these deficiencies are then almost impossible to correct in the practicing physician.

In reviewing 41 medical students at risk of dismissal from George Washington University School of Medicine, Hendron identified four distinct categories of "problem students": 1) academic problems—students with insufficient academic ability to complete successfully the curriculum, 2) intrapersonal problems—students with personal conflicts and/or excessive anxiety, 3) combined academic and intrapersonal problems, and 4) interpersonal problems—students unable to relate effectively with professors, clinicians, physicians, or patients.[4] Thirteen students (32%) fell into this fourth category. These students, whose college grade-point averages and science MCAT scores were only slightly below school averages, experienced difficulty throughout all four years of medical school, but most especially during the clinical years. In fact, only one student in the "interpersonal problem" category, a drug-abusing student reinstated by the court, graduated. Of interest, this student was subsequently dismissed from his residency for unspecified reasons. This 8% graduation rate compared to a 65% graduation rate for the problem students in the other three categories. When psychiatric treatment was offered, these students nearly always refused. Of the eight students in the entire group of 41 who threatened litigation against the school, seven were in the interpersonal problem category.

Hendron describes the maladaptive coping mechanisms in these students, which included "projecting their problems on others, denying that they had problems, lacking the appropriate anxiety necessary for satisfactory performance, and (sic) being inflexible and having strained social relationships with other students and school personnel."[4] Because of the low rate of remediation, and the litigious nature of such students, the author advises that "...the school administration should not delay in clarifying the nature of the problem and determining the student's suitability for continued medical training."[4]

Excluding residents cut only because of the pyramidal structure of a given residency program, resident dismissals are nearly always based on behavioral problems, rather than academic ones.[5] Not surprisingly, measures of moral reasoning, rather than academic performance, have been found to have the best predictive value in identifying residents viewed as "good" or "bad" by clinical faculty.[6] We all know the personal characteristics required in surgical practice that we demand in our residents—ethical and moral integrity; respect for the dignity of patients, families, and colleagues; dedication to maintaining current medical knowledge and technical skills; and an honest, ongoing self-inventory of strengths and weaknesses. We recognize and usually deal effectively with residents seen deficient in these qualities.

Ideally, potential problem physicians are weeded out through rigorous medical school and residency promotion processes. But, should such an individual slip through and enter practice, we find great difficulty in subsequently intervening. County medical societies have standing committees to assist physicians grossly "impaired" by alcohol or drug abuse. Sociopathic behavior independent of substance abuse, however, rarely generates peer-mandated professional intervention.

Why, as a profession, do we find mandated remediations or sanctions against problem physicians anathema? Several reasons seem obvious. In surgery we admire rugged independence and the willingness to face tough challenges. Those surgeons who pioneer new techniques and new technologies, and who, in operating in seemingly hopeless situations, occasionally save lives that otherwise would assuredly be lost, are among our folk heroes. In the fight against diseases losses are inevitable. Errors of commission are acceptable, but errors of omission rarely so. As each of us has made errors of judgment and technique, we are appropriately reluctant overly to judge those errors in others—"there, but for the grace of God, go you and I."

The public does not expect infallibility. What the public does expect is that, when a clear pattern of professional misconduct is obvious by the most superficial of peer reviews, such as those emanating from Quality Assurance, that we act promptly to investigate, to remediate, and, if not successful, to sanction such behavior. Courageous medical staffs and state medical boards have, on occasion, acted to exclude such miscreants. Such actions are regretfully rare. In 1987, Connecticut ranked 50th out of the 50 states (plus the District of Columbia) in the incidence of physician disciplinary actions taken by state and federal agencies in response to state medical board reviews: ten actions out of 9,853 physicians, only Montana ranked lower - 1 action out of 1,323 physicians.[7] Our failure to act decisively more frequently has made externally-mandated oversight of our profession, such as Quality Assurance and the National Practitioner Data Bank, inevitable.

Perhaps the most insightful analysis of our professional attitude, which makes effective peer review so difficult, comes from sociologists such as Charles Bosk. His 1979 study of surgical residents, *Forgive and Remember*, describes the socialization of residents, the professional attitudes towards different types of error, and the different consequences of such errors for residents and for attending surgeons.[8] Judgmental errors, for example, are considered serious infractions by residents, but attendings appear to be "insulated from rebuke."[8] The inadequate resident is dropped from the training program; the inadequate attending is privately criticized, but not publicly or professionally sanctioned.

Surgical residency training is "ethical training of the highest order,"[8] imbuing residents with a professional morality that demands an open and honest confrontation of mistakes, a morality symbolized by the "hair-shirt" ritual of the morbidity and mortality conference.[8] The highest infractions against this ethical code are to fail to confront or correct one's errors. A surgeon who does this loses the respect of colleagues and subordinates, but these sanctions do not reach the public arena. In the words of the sociologist, "There is hypertrophy of individual ethical controls, but atrophy of corporate controls."[8]

We approach surgical ethics like child rearing; we try to instill a strong ethical code in our students, our residents, and in our children, but consider it inappropriate to meddle in the affairs of practicing physicians or adult children.[8] If medical school clerkship directors, promotion committees, and residency directors fail in their disciplinary responsibilities, we are reluctant to accept that it is now our professional responsibility to intervene.

Quality Assurance is the inevitable public response, out of a sense of frustration and self-protection, to the void of public sanction within our profession. We can hardly blame the general public. Rather, we should look for ways to guarantee accuracy and sensitivity in a system that fails through oversimplification and heavy-handedness.

Bosk's analysis suggests a solution which should come as no surprise to surgeons. My chief, and your former president, Jim Foster, once told me that on a surgical service with a truly effective morbidity/mortality conference, audit committees, closed-door peer review activities (and, I would add, Quality Assurance) are superfluous. I agree. Unquestionably, the greatest benefit residency programs bring to hospitals is the ongoing inquiry and evaluation of clinical performance implicit in residency training. Residents have a special talent to ask the probing questions that make the attending staff continually evaluate their own knowledge and decision-making skills. This is best embodied in the surgical morbidity/mortality conference, with ongoing peer review in an open forum.

The appropriate role of the morbidity/mortality conference is to determine which complications are preventible and how, based on critical analysis of past performance, future patient outcomes may be improved. Raucous, petty, politically-motivated debates cannot be tolerated. A physician-specific pattern of persistent judgmental or technical errors alerts the entire department to a potential "problem physician" with an immediacy impossible in closed-door peer reviews, or in computer-generated, clerk-codified Quality Assurance statistics. There simply is no replacement for the open discussion possible in a morbidity/mortality conference to determine the quality of an individual's judgment and knowledge, and the ability of that physician to confront and accept his or her errors.

As you all know, surgical morbidity/mortality conferences are not duplicated in other specialities. We as surgeons can lead the way in *Quality Assurance* by encouraging our nonsurgical colleagues to adopt this forum as the centerpiece of physician-directed Quality Assurance. While present by Residency Review Committee mandate in all hospitals with surgical residency programs, nonteaching hospitals can also benefit from regular morbidity/mortality conferences. When necessary, additional *Quality Assurance* data gathering can refine the analysis of problems highlighted through the morbidity/mortality conference process.

Like Freudian psychology, peer review is based on the premise that dysfunctional actions are the result of incomplete self-knowledge. Once the underlying reasons for problematic behavior are identified and brought to the individual's attention, the problems will be solved. Peer review *without* the authority to impose sanctions, like Freudian psychology, fails in the face of sociopathic behavior. As stated by Bosk: "By relying on strongly-held norms that presuppose self-corrective actions we protect the inept and the immoral."[8] As unpleasant as it is, we must be willing to confront those rare individuals who view themselves as beyond societal norms, and whose actions tarnish the reputation of our entire profession.

Recognizing the litigious nature of such individuals, physicians are appropriately wary of embarking on such efforts. If hospitals *really* want Quality Assurance, and specifically, physician peer review, they need to make as explicit and complete as possible the protection they will provide to members of their medical staff, who may be sued by their colleagues for malice on the basis of adverse peer review recommendations.[9]

The question remains: Quality Assurance—How did we come to this? We came to this because we have not been diligent enough in policing our own, and thus have abdicated our responsibility to governmental and quasigovernmental bureaucrats more than willing to do so in the guise of "protecting the public health." We need to overcome our cultural bias and reaffirm peer review, including, when necessary, the imposition of meaningful sanctions. If we can restore public confidence in our ability to assure quality, then *Quality Assurance*, like other bureaucracies, will fade, with public attention and government intervention then moving on to more urgent problems.

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The Use of Intravenous Immune Globulin in Organ Transplantation

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Introduction

IMMUNE globulins are antibodies of the humoral immune system that react with specific antigens. Their reactions include opsonization of bacteria, antigen neutralization, and complement activation.[1] Immune globulin preparations have three major clinical uses: 1) replacement therapy in immune deficiency patients; 2) passive immunization; and 3) a variety of autoimmune conditions such as idiopathic thrombocytopenic purpura and autoimmune neutropenia. In addition, immune globulin has been shown to be useful adjunctive therapy for certain diseases of unknown etiology such as Kawasakis' disease. The availability of intravenous immune globulin (IVIG) since the early 1980s has led to greater use in autoimmune diseases.[2,3] IVIG use has been increasing in transplant recipients to reduce the frequency of active cytomegalovirus (CMV) infections.

CMV in the Transplant Patient

CMV disease can be classified as a primary or secondary infection.[4] Primary infection requires exposure to a source of virus and is usually more severe. Secondary infection represents reactivation of a latent CMV infection. In transplant patients, the most important source of CMV is the donor tissue or organ; transfused blood is another source of CMV. Other important factors in the development of CMV infection include the type of transplant and the intensity of immunosuppressive therapy.[4] Bone marrow transplant recipients may be particularly susceptible to CMV because of their vulnerable host immune system.[4,5] Also, some of the immunosuppressive drugs used to prevent acute graft rejection (eg, antithymocyte globulin or muromonab orthoclone [OKT-3] can reactivate latent CMV.[4,5]

The clinical manifestation of CMV infection in transplant patients can range from asymptomatic to mild (fever, malaise) to severe and life-threatening (interstitial pneumonia, secondary fungal, and bacterial infections). Also, allograft loss can occur as a result of CMV infection.[4,5]

IVIG Preparations

The World Health Organization has established guidelines to ensure consistency among IVIG products.[6] The source of IVIG is pooled, human plasma. Each unit of donor plasma is screened for a variety of pathogens, hepatitis B surface antigen, and HIV antibodies. IVIG preparations primarily contain IgG, however quantities of IgA, IgM, and IgE contaminants are also present.[1] The presence of IgG subclasses may be important for therapeutic effectiveness. Their quantities vary between products, but the clinical significance of these differences has not been determined.[7] Products containing concentrations of IgA contaminants may cause anaphylactoid reactions if administered to patients with IgA deficiency.[1] In addition, antibacterial and antiviral antibodies (eg, CMV) are found in IVIG, which may differ from batch to batch depending upon the antibody status of the donor pool.[1]

There are several IVIG products currently approved for use (Table 1).[1,8-10] It is difficult to compare these products

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reliably for several reasons: 1) they are manufactured by different processes; 2) they use different donor pools; 3) they have different Ig composition; 4) laboratory assays for evaluation are not standardized; and 5) there are no comparative clinical data to determine therapeutic equivalency. The criteria for selection of IVIG products are primarily pharmaceutical characteristics (eg, product form and storage requirements) and acquisition cost. Additional criteria are dependent upon the specific use of IVIG. For example, the CMV antibody titer may be an important criterion for prophylaxis and treatment of CMV disease in transplant recipients.[11] Recently, a hyperimmune globulin, CMV-IGIV, which is obtained from donors with high titers of CMV antibodies was approved for use in kidney transplant patients.[12] Specifically, CMV-IGIV is indicated for CMV seronegative recipients of seropositive donors. There have been no studies comparing CMV-IGIV to other IVIG preparations; but existing IVIG products, which have variable titers (high and low) of CMV antibody, have been shown to be efficacious for prevention of CMV disease in bone marrow and kidney transplant recipients.[13-15] In addition, CMV-IGIV is approximately four times more expensive than the other IVIG products.

Immune Globulin Use in Transplantation

Most studies evaluating the use of IVIG and CMV-IGIV in transplantation have been done in bone marrow or renal transplants. Transplant-associated complications in which IVIG and CMV-IGIV have shown some therapeutic and prophylactic success include:

1. Reduction in the clinical episodes of CMV disease[13-20]
2. Reduction in the development of interstitial pneumonia[14,20]
3. Decreased occurrence of septicemia and other bacterial infection[20,21]
4. Reduction in the incidence of graft versus host disease (GVHD)[20,21]
5. Decreased occurrence of hemorrhagic gastroenteritis and associated infection[18,22]

Table 1

Available IVIG Products[1,8-10]

Product	Sandoglobulin	Gammagard	Gamimune-N	Venoglobulin-I	Iveegam	Gammar-IV	Polygam
Manufacturer	Sandoz	Baxter Hyland	Cutter	Alpha Therapeutics	Immuno AG	Armour	American Red Cross
Donor Pool Source	8,000 donors	Plasmapheresis 4,000-5,000 donors	>2,000 donors	Plasmapheresis 6,000-9,000 donors	Plasmapheresis	1,000 donors	50,000 donors
IgG%	>96	>90	>98	>97	>99	>98	>99
IgG subclasses[a]							
IgG 1	60.5	67	58.7	60.9	64.1	69	57
IgG 2	30.2	25	29.3	29.4	30.3	23	29.9
IgG 3	6.6	5	6.3	5.3	4.0	7	8
IgG 4	2.6	3	5.1	4.4	1.5	2	5
IgA(ug/ml)	720	1.6	270	24	10	<20	0.74
CMV Antibody	1:52(IF) 1:2,560(ELISA)	1:1,024(HA)	1:15,019(IHA) 1:98,197(ELISA)	1:794(ELISA)			
Half-life(days)[b]	22	24	>21	29	26-29	21	24
Product form	lypholized	lypholized[c]	solution	lypholized	lypholized[c]	lypholized	lypholized[c]
Storage	room temp	room temp	refrigeration	room temp	room temp	room temp	room temp

Key:

a. mean % of total IgG

b. IVIG half-lives can vary between different types of transplants due to unknown mechanisms

c. administration filter required

IF= Immunofluorescence assay
ELISA= Enzyme-linked immunosorbent assay
HA= Hemagglutination
IHA= Indirect Hemagglutination

6. Reduction in the occurrence of leukopenia and abnormal liver function tests[14,22,23]

Although no study has yet identified the optimum dosage, length of therapy, or preparation of choice for use in transplant patients, some important points regarding CMV infection and immune globulin use in transplantation include:

1. For CMV seronegative patients, primary CMV infection can be reduced by screening donor tissue and blood products. For a seronegative recipient receiving CMV seronegative donor organ and having few blood transfusions, there is a low risk for CMV infection. There is no clear indication for IVIG use in these patients.
2. If the donor is CMV seropositive, then IVIG may have a role in reducing symptomatic infection. There is greater justification for use in transplants where graft loss mortality or CMV morbidity is expected to be higher (eg, bone marrow, liver, heart, or heart-lung transplants). Our current recommendation for prevention of CMV disease (and GVHD) is IVIG 200-400mg/kg on days 25, 50, and 75 after transplantation, and 200mg/kg on day 100 after transplantation.
3. Seropositive graft recipients almost always experience reactivation of latent CMV infections. The significance of secondary infections is usually related to the degree of immunosuppression and/or the immunosuppressive regimen used. However, one cannot confidently predict the severity of infection based on the immunosuppressive regimen or dosage. There may be a higher frequency of CMV infections when antithymocyte globulin or muromonab orthoclone is used for acute rejection therapy. Although definitive regimens and outcomes have not been established, the use of IVIG in this clinical setting is probably warranted. Our current recommendation for treatment of CMV disease is IVIG 400mg/kg on days 1, 2, and 7 in combination with gancyclovir.

Summary

There are no comparative clinical data to differentiate the available IVIG products. Cost, pharmaceutical considerations, and CMV titers are criteria for selecting these products. CMV-IGIV has higher titers of CMV antibodies but is more costly.

The potential for CMV infection in transplant patients is great, but the clinical significance may vary. Likewise CMV morbidity and mortality is variable and dependent on the type of transplant, the donor, and immunosuppressive regimens used. IVIG has a role in decreasing CMV infections in transplant patients, but further study and cost-benefit analysis is necessary to determine optimal regimens.

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CONSENSUS CONFERENCE

Clinical Use of Botulinum Toxin

NATIONAL INSTITUTES OF HEALTH

Introduction

BOTULINUM toxin is a complex protein produced by the anaerobic bacterium *Clostridium botulinum*. Previously known only as a cause of a serious and often fatal paralysis acquired through ingestion of contaminated food, the toxin causes paralysis by blocking the presynaptic release of acetylcholine at the neuromuscular junction. Advantage can be taken of this neuromuscular blocking effect to alleviate muscle spasm due to excessive neural activity of central origin or to weaken a muscle for therapeutic purposes. In therapeutic applications, minute quantities of botulinum neurotoxin type A are injected directly into selected muscles.

Local injections of botulinum toxin are effective in the treatment of strabismus, essential blepharospasm, and hemifacial spasm. The Food and Drug Administration recently has approved botulinum toxin for these indications. Clinical studies indicate that botulinum toxin injections also can provide useful symptomatic relief in a variety of other conditions characterized by involuntary spasms of certain muscle groups, notably in focal or segmental dystonia including spasmodic torticollis, oromandibular dystonia (orofacial dyskinesia, Meige syndrome), and spasmodic dysphonia. A few studies suggest that it also may be useful in treating writer's cramp and related occupational cramps of the hand, limb dystonia, anismus, and urinary detrusor-sphincter dyssnergia. The value of the toxin in treating other conditions such as spasticity due to brain or spinal cord lesions is under investigation.

For most patients with these conditions, botulinum toxin injection provides significant but variable relief of symptoms that lasts for weeks to months. Repeated injections are required to sustain benefit over long periods of time. Conventional therapy for many of these conditions depends on minimally effective drugs or surgical procedures designed to denervate or destroy the involved muscles and has been generally unsatisfactory. Reports of the benefits of botulinum toxin have thus aroused great interest and hope among physicians, biomedical scientists, and patients.

This new therapeutic agent has been used principally by highly specialized physicians in academic medical centers. Many of the data are recent. Controversies persist regarding the indications, contraindications, optimal methods of use, and the nature of the side effects. Long-term effects of chronic botulinum toxin therapy are unknown. Long-term follow-up of treated patients is necessary. Additonal research appears needed to clarify the metabolism and pharmacology of the toxin, assess new indications, and define optimal techniques of administration.

To evaluate the developing experience with botulinum toxin in the treatment of various clinical disorders characterized by muscle hyperactivity, the National Institute of Neurological Disorders and Stroke and the Office of Medical Applications of Research of the National Institutes of Health convened a consensus development conference on 12-14 November 1990. The conference was cosponsored by the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health and the Food and Drug Administration. After a day and a half of presentations by experts from all

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NIH Consensus Development conferences are convened to evaluate available scientific information and to resolve safety and efficacy issues related to a biomedical technology. The resultant NIH Consensus Statements are intended to advance understanding of the technology or issue in question and to be useful to health professionals and the public.

NIH Consensus Statements are prepared by a nonadvocacy, nonfederal panel of experts based on (1) presentations by investigators working in areas relevant to the consensus questions during a $1\frac{1}{2}$- day public session; (2) questions and statements from consensus attendees during open discussion periods that are part of the public session; and (3) closed deliberations by the panel during the remainder of the second day and the morning of the third day. This statement is an independent report of the panel and is not a policy statement of the NIH or the federal government.

From the Office of Medical Applications of Research, National Institutes of Health, Bethesda, Md.

over the world and discussion by the audience, a consensus panel drawn from specialists in relevant fields, clinical investigators, and public representatives considered the evidence relative to the following questions:

1. What are the mechanisms of actions of botulinum toxin?
2/3. What are the indications and contraindications of botulinum toxin therapy?
4. How should it be handled to assure safe and effective use?
5. What are its side effects and complications?
6. What further research on botulinum toxin therapy is needed?

1. What Are the Mechanisms of Action of Botulinum Toxin?

There are several serologically distinct botulinum neurotoxins, which have slightly different specific effects. Only botulinum neurotoxin type A has been used in clinical studies at present. There are three steps in the neurotoxic action. First the toxic protein attaches to the presynaptic nerve membrane. Then the toxin crosses the presynaptic plasma membrane, following which the toxin inhibits release of vesicle-bound acetylcholine. The specific mechanism of intracellular action in blocking the release of acetylcholine and the subsequent fate of the toxin are not known at present. Although botulinum toxin has been shown to enter the central nervous system in animals by retrograde axonal transport, the therapeutic effects in humans are due primarily to the blockade of peripheral neuromuscular transmission.

Botulinum toxin produces its therapeutic effect by a long-term blockade that leads to changes very similar to those produced by surgical denervation. These changes include muscle paralysis, atrophy, and electromyographic abnormalities. In most situations, the clinical effects of botulinum toxin are of limited duration. In experimental animals and humans, recovery is accompanied by sprouting of new nerve terminals. The formation of new neuromuscular junctions adjacent to these sprouts parallels the effective return of neuromuscular activity.

2 and 3. What Are the Indications and Contraindications for the Use of Botulinum Toxin Treatment?

Introduction

Botulinum toxin therapy is invasive. Its use should be reserved for patients in whom a diagnosis has been established with reasonable certainty. Botulinum toxin is safe and effective for the symptomatic treatment of blepharospasm, strabismus, hemifacial spasm, adductor spasmodic dysphonia, cervical dystonia (spasmodic torticollis), and jaw-closing oromandibular dystonia. Botulinum toxin is promising in the management of other conditions, including other oromandibular dystonias, focal and segmental limb dystonias, abductor spasmodic dysphonia, stuttering, and vocal and other tremors. Preliminary studies suggest that botulinum toxin injection may be useful in urinary and anal sphincter dysfunction, spasticity, and dynamic deformities in selected cases of cerebral palsy.

Contraindications to the use of botulinum toxin are allergy to the drug and infection of inflammation at the propsosed injection site(s). Safety for use during pregnancy or lactation has not been established. Therefore, it is prudent to avoid botulinum toxin therapy for elective procedures in women of childbearing age until absence of pregnancy or adequate contraception is assured. Relative contraindications include diseases of neuromuscular transmission, coagulopathy (including therapeutic anticoagulation), and inability of the patient to cooperate. In the more complex disorders, botulinum toxin therapy should not be used unless a skilled interdisciplinary team and sophisticated instrumentation are available to ensure valid diagnosis, state-of-the-art treatment, and appropriate follow-up. The physician administering this drug should be trained in its use and qualified to manage any complications.

I. Ophthalmic Disorders

Extraocular Muscle Dysfunctions.—Strabismus is a misalignment of the eyes that may result in diplopia (double vision), suppression and amblyopia (lazy eye), deficient depth perception, and an undesirable appearance.

Botulinum toxin is effective as an alternative to surgery to realign the eyes of selected patients with congenital or acquired strabismus. The toxin appears to be more effective in esotropia (in-turning of the eyes) of small to moderate angles than in exotropia (out-turning), vertical deviations, or large angle deviations. Botulinum toxin may be indicated in certain ocular conditions where surgery is inappropriate, such as acute thyroid ophthalmopathy. Controlled studies comparing botulinum toxin treatment and surgical treatment of strabismus have not been done.

Botulinum toxin may prevent contracture of antagonist muscles in cases of extraocular muscle palsy from which some recovery is expected. In these cases, single binocular vision may be enabled or enhanced during the recovery phase, and late contractures that would require surgery may be prevented. The drug also may be used as an adjunct to surgery intraoperatively and postoperatively.

Disadvantages of botulinum toxin in the extraocular muscles include the need for more than one injection, unstable ocular alignment for several weeks, diplopia, and blepharoptosis. Other complications may occur, such as perforation of the globe and orbital hemorrhage. Administration of the toxin requires electromyographic control and injection by a physician trained in the technique.

Blepharospasm.—Essential blepharospasm is a variable, progressive, bilateral, involuntary, focal dyskinesia characterized by spasmodic, forceful eyelid closure resulting in visual disability. The disorder may be associated with cranial-cervical dystonia (Meige syndrome).

Botulinum toxin is effective in the long-term management of patients with essential blepharospasm, and it has become the treatment of choice. Symptoms are controlled in most patients by injection of the toxin in multiple sites in the periocular and facial muscles. Duration of control is variable but averages between three and four months. Timing for repeat injections is determined by the patient's sense of need and the physician's estimation of recovery of muscle function. Injection sites and dosages vary widely in published reports, but treatment results seem to be similar. Injections in these areas are given without electromyography control in most cases.

II. Neurological Disorders

Introduction.—Botulinum toxin treatment of neurological conditions requires proper identification of the pathologically hyperactive muscles, either by inspection and palpation or by electromyography. Not all patients respond to botulinum toxin injection. In focal dystonias, most of which respond poorly to conventional therapy, botulinum toxin injecitons may be the treatment of choice. In more generalized dystonias, however, oral medication may be tried before botulinum toxin. In generalized disorders, botulinum toxin injection is indicated only for the treatment of particularly severe focal abnormalities, because injection of multiple muscle groups would require unacceptably high doses of toxin.

Hemifacial Spasm.—Hemifacial spasm is characterized by sudden, unilateral, synchronous contractions of muscles innervated by the facial nerve. These may subside immediately or persist as a tonic contraction of several seconds' duration and may occur many times a day. Eyelid closure may interfere with vision on the involved side. Hemifacial spasm may cause discomfort, cosmetic deformity, and social embarrassment. In most cases, it is due to mechanical irritation of the facial nerve in the posterior fossa or distally. Palliation with repeated injections of botulinum toxin may be appropriate and effective. Oral medications and surgical decompression are therapeutic alternatives.

Cervical Dystonia.—Cervical dystonia (spasmodic torticollis) is characterized by asymmetric muscle spasms in the neck, which cause turning or tilting movements and sustained abnormal postures of the head. Mild to moderate head tremor and musculoskeletal pain are frequently present. The spasms often subside briefly in response to a variey of stimuli. Spontaneous remission may occur. Some patients respond to a limited extent to various medications, but many do not. Botulinum toxin is an accepted therapy.

Oromandibular Dystonia.—Oromandibular dystonia (orofacial dyskinesia, Meige syndrome) consists of continuous, bilateral, asynchronous spasms of muscles of the face, jaw, pharynx, tongue, and, in some severe cases, neck, larynx, and respiratory system. It may respond to a modest degree to treatment with anticholinergics, baclofen, benzodiazepines, and other medication. Treatment with botulinum toxin has been shown to be effective and safe in the "jaw-closing" variant of the condition. "Jaw-opening" and other more complex variants also may respond to botulinum toxin injection. Optimal management of oromandibular dystonias requires thorough knowledge of the anatomy and pathophysiology as well as collaboration among an experienced otolaryngologist, speech-language pathologist, neurologist, and physicians skilled in regional electromyography. Because many muscles often are involved, multiple injections may be required. Side-effects, including dysphagia, dysarthria, diplopia, and weakness, may occur. Further studies of the effectiveness of botulinum toxin in these conditions are needed.

Focal and Segmental Limb Dystonias.—Focal and segmental limb dystonias consist of involuntary, inappropriate spasms of limited numbers of distal limb muscles. The spasms are often precipited by voluntary contractions and include occupational dystonias such as writer's cramp and musician's cramp. These dystonias can be incapacitating and have been exceptionally resistant to treatment with oral medications. Preliminary clinical reports indicate that botulinum toxin may be effective therapy, but further studies are necessary.

Anismus, Urinary Detrusor-Sphincter Dyssynergia, and Spasticity.—Anismus is a rare condition in which dyssynergia of the external anal sphincter and puborectalis muscles causes profound constipation. Urinary detrusor-sphincter dyssynergia following spinal injury is characterized with bladder contraction. The result is urinary obstruction. Spasticity is excessive muscle tone caused by lesions of the corticospinal tract. Preliminary clinical reports suggest that botulinum toxin may be useful in these conditions.

III. Voice and Speech Disorders

Introduction.—Botulinum toxin therapy for voice and speech disorders requries the involvement of an interdisciplinary team, including an otolaryngologist, speech-language pathologist, neurologist, and a physician skilled in regional electromyography. A psychiatrist and/or psychologist, voice scientist, and neuroradiologist should be available. Voice laboratory facilites should be available to assure valid diagnosis and to document and quantify voice and speech function before and following treatment. In addition, the team should make available to the patient other treatment such as voice and speech therapy.

Adductor Spasmodic Dysphonia.—Predominantly adductor spasmodic dysphonia is characterized by forceful, involuntary approximation of the vocal folds. This interrupts the airstream and produces a strained, hoarse, choppy voice. Botulinum toxin therapy is effective in ameliorating the symptoms and restoring fluency. Because the effect is temporary, repeated injections are required.

Abductor Spasmodic Dysphonia.—Predominantly abductor spasmodic dysphonia is a condition characterized by forceful, involuntary separation of the vocal folds. This causes breathy interruptions in speech. Botulinum toxin therapy has been reported to be effective in selected cases, but it carries a risk of bilateral abductor paralysis with airway obstruction if the posterior cricoarytenoid muscles are injected.

Stuttering and Vocal Tremor.—Stuttering is characterized by repetitions of sounds and words, prolongations of sounds, and interruptions of the fluent flow of speech. Vocal tremor is characterized by quavering because of adductor and abductor oscillations of the vocal folds. Preliminary reports of botulinum toxin therapy for each of these conditions warrant further research.

4. How Should it Be Handled to Assure Safe and Effective Use?

Commercial preparations of botulinum toxin include nontoxin protein and other stabilizers, notably albumin pasteurized to kill the hepatitis and human immunodeficiency viruses. Paracrystalline stability for greater than two years has been established. For administration, this material is diluted to an appropriate concentration in preservative-free normal saline.

Local injection of pure toxin does not cause irritation or inflammation. The occasional complaints of pain at the site of injection may be related to factors such as the volume injected, concentration of active (or inactive) protein, or even the pH of the solution; however, no studies have investigated these variables.

The appreciation of botulinum as a potent, irreversible, and potentially lethal neurotoxin is fundamental to the safe use of this natural product. No pharmaceuticals currently are available to overcome the blockade created by botulinum toxin at the neuromuscular junction. However, coincident administration of agents known to potentiate neuromuscular blockade, such asaminoglycosides, should be avoided.

Single large doses of greater than 500 mouse units (MU) of botulinum may produce acute symptoms and signs of botulism. There is no evidence of desensitization with chronic use.

In additon to diagnostic prudence, elaborate planning and precise understanding of three-dimensional anatomy of the regions of proposed injection are essential for safe administration. Physicians who attempt this therapeutic intervention must assume the joint responsibilities of knowledgeable diagnostic evaluation and diligent follow-up of their patients.

Even small volumes of botulinum toxin may have undesired regional effects, presumably because of diffusion. Injection of smaller volumes of more concentrated toxin may limit regional side effects. For example, injection of the sternocleidomastoid, lingual, and deep neck muscles can be associated with weakness of the pharyngeal and esophageal muscles and resultant difficulty with swallowing. Similarly, adjacent levator muscle paresis is seen in 10 to 40% of cases in whom the orbicularis oculi muscle is injected. Although dysphagia and blepharoptosis seem to be shorter lived than the paralysis of the target muscles, these complications are sometimes troublesome.

Routine electromyography is not required in every patient. However, the injection of muscles that are difficult to identify, such as those in the orbit, the larynx, and the pterygoid area, and any muscle in obese subjects, is best accomplished with simultaneous hollow needle electrode recordings. Direct visualization of the target, such as the extraocular muscles during surgery or the larynx by indirect laryngoscopy, may obviate the need for electromyography in selected circumstances.

Prudent and current medical practice dictate that the patient or individual responsible for legal consent should be informed of all reasonable medical and surgical alternative therapies, the possibility of limited or absent benefits, the lack of permanent response and the unpredictability of response to an individual dose, and the need for repeated administration. For specific applications, other considerations should be disclosed. For example, in ophthalmic applications, scleral perforation, orbital hemorrhage, blepharoptosis, and overcorrection due to weakness of other extraocular muscles may occur. When the larynx is injected, bleeding and laryngeal edema, hoarsenesss, breathiness, and even aspiration may follow. When the deep neck musculature is injected, weakness and difficulty in swallowing can occur.

5. What are its Side Effects and Complications?

Botulinum toxin is a safe therapy when administered in the appropriate doses by experienced physicians. Side effects are generally transitory, well tolerated, and amenable to treatment. Persistent complications are distinctly rare, and serious side effects are uncommon. Generalized weakness, mimicking botulism, is rare, but electromyographic abnormalities may occur in muscles distant to the site of injection without clinical signs of muscle weakness. Systemic complications are ucommon, but several studies report a flu-like syndrome, particularly after the first injection. A similar syndrome has been reported following placebo injection. Most complications are related to diffusion or, rarely, inadvertent injection of the toxin into nearby muscle groups. Some complications may be dose dependent.

Some patients develop antibodies to the toxin. It is unclear exactly what factors predispose to development of antibodies, but some studies suggest that risk is increased by the administration of more than 300 MU within a 30-day period and by low body weight of the patient. Antibodies may be one factor associated with therapeutic failure. The long-term (> five years) effects of chronic botulinum toxin injections are unknown.

Complications of therapy for specific disorders have been reported in large clinical studies and in a few, small, placebo-controlled studies. Although the types of complications are consistent from study to study, the rates vary, reflecting differences in technique and methods of data collection. Complications are described according to site of injection and clinical disorder.

Blepharospasm, Strabismus, and Hemifacial Spasm.—For blepharospasm, mild eyelid ptosis is the most common complication (10 to 40% of cases). Ptosis usually resolves within a few weeks and may be dose or site related. Severe ptosis and diplopia are estimated to occur in 3% and 6% of patients, respectively. Other infrequent local complications include ectropion and lagophthalmos leading to exposure keratopathy and tearing. Facial weakness, ecchymoses, and eyelid edema also may occur. Treatment of strabismus frequently is complicated by transient ptosis and undesirable weakness of other extraocular muscles. More severe complications, such as perforation of the globe and orbital hemorrhage, have occurred. In hemifacial spasm, the types of compli-cations are similar to those that occur in blepharospasm. In addition, injection of muscles that elevate the lip may result in bothersome weakness.

Cervical and Oromandibular Dystonias (Meige syndrome) and Spasmodic Dysphonias.—The most common complications of toxin injection for cervical dystonias are dysphagia, local neck weakness, and local pain. These are generally short-lived, but dysphagia occasionally is severe enough to require a modified diet and monitoring for aspiration. Risk for complications is higher in women, individuals with thin necks, those with low body weight, and those receiving injections into the sternocleidomastoid muscles. Treatment of oromandibular dystonias has similar complications. Dysphagia is common when injections are given into the pterygoid and deep tongue muscles, and aspiration may occur. Patients with spasmodic dysphonias also are subject to transient dysphagia. "Breathiness" of voice is seen in up to 50 % of patients and occasionally is severe enough to warrant discontinuation of treatment. Hoarseness and aspiration also may occur.

Hand and Limb Dystonias.—Mild local weakness, a desired effect, occurs in all patients who are treated successfully with toxin for hand and limb dystonias. However, until the appropriate dose is determined for an individual patient, weakness may be excessive. Transitory tenderness at the site of injection is noted in up to 20% of patients.

Other Conditions.—In a small clinical series, toxin treatment for detrusor-sphincter dyssynergia in spinal cord injury patients has been uncomplicated except for mild, transitory, generalized weakness in two patients. Treatment of focal spasticity in multiple sclerosis and cerebral palsy, in small case series, has been uncomplicated. Transitory fecal incontinence has been recorded in two of 15 patients treated for anismus.

6. What Further Research on Botulinum Toxin is Needed?

I. To study the general properties of botulinum toxin, including:
  - mechanism of action
  - metabolism and catabolism
  - mechanisms of recovery from paralysis
  - the target receptors
  - pharmacology of other serotypes
  - antidotes and blocking techniques
  - techniques to increase the specificity and duration of action
  - stability and consistency of pharmaceutical preparations

II. To study the indications for botulinum toxin treatment, including:
  - efficacy and safety through controlled clinical trials that use reliable outcome measures
  - optimal measures of clinical benefit
  - long-term and remote effects
  - dose/response relationships and dose schedules
  - causes of primary failure
  - causes of secondary failure
  - pathophysiology of the diseases treated
  - physiology of spasm reduction in regional muscles that are not directly injected

III. To study contraindications for botulinum toxin treatment, including:
  - pregnancy and lactation

- high doses or chronic maintenance in infants and children
- diseases of neuromuscular transmission

IV. To study the technique of injecting and handling of botulinum toxin, including:
- effects of location, dose, concentration, and volume on response
- dose selection based on objective physiologic or anthropometric parameters
- the value of electromyography for diagnosis, localization of the site(s) of administration, and control of dose

V. To study the side effects and complications of botulinum toxin treatment, including:
- antibody formation and its implications
- long-term consequences of repeated injection
- the variability in sensitivity to injection among different patients and different muscle groups in an individual patient
- the mechanism of undesirable regional effects
- valid and reliable parameters for assessment of outcome
- systemic effects

Conclusions and Recommendations

1. Botulinum toxin therapy is safe and effective in the treatment of strabismus and in the symptomatic treatment of essential blepharospasm, hemifacial spasm, predominantly adductor spasmodic dysphonia, jaw-closing oromandibular dystonia, and cervical dystonia.
2. Botulinum toxin therapy appears promising in other conditions described in this report, but additional investigations, including controlled clinical trials, are needed.
3. Botulinum toxin therapy is not curative in chronic neurological disorders.
4. Further study of the mechanism of action of botulinum toxin and its pharmacotherpeutics is needed.
5. International standardization of measures of biological activity of botulinum toxin is needed.
6. For most indications, botulinum toxin should be used by committed interdisciplinary teams of physicians and related health care professionals with appropriate instrumentation.
7. The safety of botulinum therapy during pregnancy, breast feeding, and chronic use in childhood is unknown.
8. The long-term effects of chronic treatment with botulinum toxin remain unknown. Prolonged follow-up is necessary in patients on maintenance therapy. An independent national database should be established.
9. The health care community needs additional education for the availability, benefits, risks, and special health care provider skills associated with botulinum toxin therapy.
10. Further clinical and basic research should be encouraged to address the many unanswered questions about botulinum toxin and its therapeutic uses.

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Andrew Blitzer, M.D., and Mitchell F. Brin, M.D.: "Botulinum Toxin for the Treatment of Oromandibular and Lingual Dystonia"

Mitchell F. Brin, M.D., and Andrew Blitzer, M.D.: "Botulinum

Toxin for the Treatment of All Forms of Spasmodic Dysphonia"

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Botulinum Toxin in the Management of Essential Blepharospasm: Clinical Trials 2"

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John S. Elston, M.D., B.Sc., F.R.C.S.: "Botulinum Toxin for Blepharospasm: Rationale and Results"

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Ultrasonic Imaging of the Abdomen

Report of the Ultrasonography Task Force

AMA COUNCIL ON SCIENTIFIC AFFAIRS

As new imaging modalities emerge and existing technologies improve, indications for a particular imaging method may change. This article examines current indications for abdominal and prostatic ultrasound examination and, where possible, compares ultrasound with other imaging techniques. This is not an attempt to list all possible ultrasound indications or examinations, but rather an attempt to serve as an aid to informed imaging selection based on current literature and equipment.

ULTRASONOGRAPHY is the least expensive cross-sectional abdominal imaging modality. Ease of transportability and lack of ionizing radiation make ultrasonography valuable for imaging the unstable or pregnant patient. Real-time ultrasonography allows easy identification of motion, such as bowel peristalsis and diaphragmatic movement. Doppler equipment, including color, has made noninvasive vascular imaging of the abdomen a safe and inexpensive alternative to angiography. Transrectal sonography of the prostate has added another dimension to diagnosis of diseases of the prostate and periprostatic tissues.

However, despite equipment improvements, ultrasonography imaging limitations remain—most important is the high level of operator dependence. Consistently accurate results can be expected only if the examiner and interpreter have had adequate training and maintain these skills through frequent use.

Gas-containing bowel and bony structures are impenetrable barriers to the sound beam. Wounds, bandages, and sutures may prevent good skin contact. For the traumatized patient, ultrasonography is unable to provide the vital global evaluation of bony and soft-tissue structures attainable with computed tomography.

Abdominal Wall

A mass clinically suspected of being within the abdominal wall can be easily and accurately evaluated by ultrasonography, which can differentiate fluid collections such as abscesses or seromas from solid neoplasms. Clinically suspected rectus sheath hematomas can be confirmed when a fluid-filled or complex mass is found. Ultrasonography is indicated to guide needle aspiration of nonpalpable abdominal wall lesions if abscess of malignant neoplasm is suspected. Abdominal wall defects can be identified even in the absence of protruding, peristalsing bowel.[1]

Abdominal Fluid Detection

Ultrasonography is sensitive and specific for the detection of ascites.[2] If infection or malignant neoplasm is suspected as the cause for ascites, ultrasonography is important for fluid localization for paracentesis.

Ultrasonography is indicated for abdominal abscess

From the Council on Scientific Affairs, American Medical Association, Chicago, Ill.

This report was presented to the House of Delegates of the American Medical Association on June 24, 1990, as an informational report of the Council on Scientific Affairs.

This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all facts and circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and patterns of practice evolve. This report reflects the scientific literature as of March 1990.

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detection and is the most rapid means of imaging the debilitated patient who is too unstable to travel to the radiology department. The right upper quadrant, left upper quadrant, and true pelvis are the areas of highest sensitivity because of the acoustic paths afforded by the liver, spleen, and distended urinary bladder, respectively. Because there is overlap between the sonographic appearance of abscesses and other lesions, such as hematoma, biloma, or seroma, aspiration of fluid for bacteriologic examination is often necessary.

Ultrasonography is especially useful for abscess detection when directed to a specific location by clinical signs and symptoms. However, studies have frequently demonstrated the ability of computed tomography to delineate more abscesses, especially in areas difficult or impossible to see with ultrasonography.[3,4] If ultrasonography and computed tomography studies are equivocal, scanning with indium 111-labeled leukocytes or gallium 67 may be valuable. These studies have the added ability to localize an extra-abdominal site as a source of sepsis. The chief disadvantage of these imaging methods is the 6- to 24-hour delay necessary for tracer localization to an abnormal area.

Percutaneous abscess drainage has become an indispensable tool in the care of the patient with sepsis. Often, the choice of guidance method depends most on the experience of the radiologist performing the drainage procedure. Ultrasonography guidance is often used if a known fluid collection is superficial, if a suitable access route is known, or if the patient is unable to be moved to a computed tomography scanner or fluoroscopy suite. Computed tomography is valuable if negotiation of a safe drainage tract past an intervening organ cannot be assured with real-time ultrasonography.

Liver Parenchyma

Ultrasonography is well suited to liver evaluation since the liver itself usually serves to displace gas-containing bowel from the anterior and right abdominal walls. Hepatic and portal venous branches are easily identified and serve as an accurate guide to liver anatomy.[5] Ultrasonography can easily differentiate true hepatic enlargement from a normal-sized but inferiorly displaced liver, as is found with emphysema.

Ultrasonography is indicated for examination of the patient suspected of having diffuse hepatocellular disease, because diffusely increased or diminished liver echogenicity or increased portal vein wall echogenicity is specific for this diagnosis.[6,7]

Ultrasonography may also help to differentiate a fibrofatty from a centrilobular process.[6] Unfortunately, increased liver echocardiography (echo) brightness seems best related to increased fat content, both in processes associated with fibrosis and in fatty infiltration.[8] Histologic biopsy studies, therefore, remain necessary to differentiate reversible from nonreversible (fibrous) liver injury[6-8] and to exclude the possibility of unusually diffuse malignant disease, as is seen with hepatocellular carcinoma.

Ultrasonography is less sensitive than liver-spleen scintigraphy in the diagnosis of mild hepatocellular disease. Indeed, most patients with acute viral hepatitis demonstrate normal liver echo patterns. However, both ultrasonography and computed tomography are more useful than scintigraphy in searching for findings associated with cirrhosis and portal hypertension such as ascites, varices, and paraumbilical vein recanalization.

Because of low cost and ready availability, ultrasonography maintains a place in the evaluation of suspected metastatic liver disease.[9] Ultrasonography can identify most patients with metastatic disease[9] and can serve to guide biopsy procedures of even tiny lesions. However, recent contrast-enhancement computed tomography techniques and emerging magnetic resonance imaging (MRI) sequences leave no doubt that these procedures can identify more liver lesions in more patients than can conventional ultrasonography.[9] Therefore, if the results of ultrasonography are normal, incomplete, or unsuccessful, additional but more expensive or invasive imaging must be considered. If ultrasonography demonstrates potentially resectable disease, the highest-quality complementary study (computed tomography or MRI) available must be performed to prevent unnecessary or inappropriate resection.

The greatly increased sensitivity that occurs when the ultrasound transducer can be placed directly on the liver during surgery can frequently yield information that alters the operative approach during resection of liver tumors.[10]

Ultrasonography is useful in identifying hepatocellular carcinoma and may be of special value in determining small lesions.[11] It can also be accurate in screening for hepatocellular carcinoma in high-risk populations and is especially well suited to identifying intravascular tumor spread. However, computed tomography may be more valuable in definition of tumor margins when resection is contemplated. Although tumor invasion of hepatic vessels and high-velocity tumor blood flow found on Doppler ultrasound studies strongly suggest hepatoma,[12] there are no definitive tissue-specific ultrasonography findings (nor are there for other imaging modalities). Because hepatocellular carcinomas may have varied ultrasonography findings—including diffuse liver echo irregularity and hypoehcoic, hyperechoic, or mixed patterns[11]—it may be impossible to differentiate hepatocellular carcinoma from other liver lesions, and biopsy studies are usually necessary.

Cholangiocarcinoma presents a varied ultrasonography appearance, and a specific tissue diagnosis based on such studies is not possible. However, ultrasonography is more accurate than computed tomography in demonstrating a polypoid intraductal tumor and is, therefore, complementary to computed tomography and cholangiography for treatment planning.

Ultrasonography can diagnose simple hepatic cyst, if the criteria of no internal echoes, smooth, thin walls, and acoustic enhancement on the far side of the cyst are met.

Ultrasonography is sensitive and specific in the search for intrahepatic abscess. However, some abscess ultrasonography features are shared with complicated hepatic cysts, necrotic tumors, hematomas, and, occasionally, solid tumors. When suspected abscess is found, ultrasonography guidance can rapidly and safely be used for diagnostic confirmation and drainage.

Ultrasonography can demonstrate findings suggestive of liver hemangioma, especially with smaller lesions.[13] In many patients, however, other imaging modalities, including dynamic computed tomography, technetium-labeled red blood cell scintigraphy, MRI, angiography, or biopsy may be necessary for hemangioma confirmation.[14,15]

Ultrasonography is of value in the diagnosis of focal fatty infiltration of the liver; it can be especially useful to monitor the resolution of these lesions over time.[16] Computed tomography and liver scintigraphy are complementary and often necessary studies to aid ultrasonography in this diagnosis.[16] In atypical cases of suspected focal fatty infiltration of the liver, especially in the setting of a known extrahepatic primary malignant neoplasm, biopsy may be necessary.

Biliary Tree

Ultrasonography is indicated as an initial imaging study for the jaundiced patient because of its specificity in identification of dilated biliary ducts. By use of real-time equipment and multiple patient positions, the level can be accurately identified in approximately 90%, and the origin suggested in 70% to 88%, of patients with biliary obstruction.[17,18]

Unfortunately ultrasonography examination may miss portions of the biliary system in as many as 73% of patients suspected of having biliary tract disease.[19] If ultrasonography evaluation of bile ducts is limited, computed tomography with intravenous contrast or scintigraphy with technetium-labeled lidofeninlike compounds may be helpful. However, if intravenous contrast cannot be administered because of contrast sensitivity or renal insufficiency, dilated biliary ducts may be difficult to distinguish from portal venous branches using computed tomography.

Sclerosing cholangitis and desmoplastic malignant neoplasms may prevent ductal dilatation in the presence of obstruction. If obstruction is partial or early, ducts may not yet be dilated, and these situations may, therefore, lead to false-negative computed tomography or ultrasonography examination. In these situations hepatobiliary scanning with technetium-labeled lidofeninlike compounds or direct opacification by transhepatic or endoscopic means may confirm or rule out abnormality.

The detection rate of common duct stones by ultrasonography varies widely in the literature, from 5% to 80%.[17,19] Ultrasonography is clearly less sensitive if ductal dilatation is not present. In one study of patients subsequently proven to have choledocholithiasis, 77% had stones visible with ultrasonography within dilated ducts, but in only 12% of patients with nondilated ducts could common duct stones be identified.[20] Therefore, if suspected common duct stones are not identified by ultrasonography or computed tomography, direct visualization of the biliary tree with percutaneous cholangiography or endoscopic retrograde cholangiography is indicated.

Hepatic Vasculature

The acoustic window afforded by the liver allows easy access for sonographic evaluation of hepatic vessels. Vessels can be evaluated for filling defects, such as thrombus or tumor, and evidence of collateral flow. Portions of the portal venous system can be visualized in virtually 100% of subjects.[19] The hepatic veins and the hepatic artery can be seen in most patients. By use of Doppler equipment, presence of blood flow as well as direction and velocity can be evaluated. The advent of color flow imaging has improved the ease with which Doppler imaging can be used and in many situations has improved overall accuracy.

Since confirmation of portal vein patency is crucial before liver transplantation, and hepatic artery, portal vein, and inferior vena cava occlusion are important complications of this operative procedure, color Doppler imaging has become important in the examination of these patients.[21]

Gallbladder

Oral cholecystography and ultrasonography are the most common methods used to diagnose the condition of patients suspected of having nonacute gallbladder disease. Ultrasonography has replaced oral cholecystography in most radiology departments because of ease of examination and lack of ionizing radiation. The examinations are approximately equal in sensitivity for the detection of gallbladder disease.[22] Many studies, however, have demonstrated the superiority of ultrasonography over oral cholecystography in stone detection.[23] Oral cholecystography is less expensive, but since gallbladder ultrasonography should be performed as a part of a global abdominal sonogram, ultrasonography adds the ability to detect other abnormalities apart from the biliary tree. Although oral cholecystography is more sensitive for the diagnosis of adenomyomatosis and cholesterolosis, it remains unclear how these diseases relate to patients' symptoms. Ultrasonography is the only means of detecting biliary sludge, which may lead to gallstones in some patients.

Ultrasonography and hepatobiliary scanning are the primary methods of diagnosing the condition of the patient suspected of having acute cholecystitis. Scintigraphic diagnosis is primarily based on lack of filling of the gallbladder with tracer on delayed images, thereby confirming an obstructed cystic duct. Ultrasonography findings associated with cholecystitis include gallstones and other abnormal intraluminal contents, wall abnormalities, pericholecystic fluid, and pain exactly at the site of the gallbladder (positive ultrasonography Murphy's sign).[24,25]

Scintigraphic sensitivity and specificity are both typically reported as greater than 90%. There is great variation in the criteria for ultrasonography diagnosis of acute cholecystitis in the literature; most comparisons demonstrate somewhat lower specificity for ultrasonography.[26,27] If gallbladder wall thickening or gallstones alone are the sonographic criteria, the specificity is low because either may commonly be found in asymptomatic patients. The combination of stones and wall thickening, especially in conjunction with a positive Murphy's sign on ultrasonography, has demonstrated accuracy similar to that obtained with scintigraphy.[24]

Current surgical opinion favors urgent cholecystectomy for acute cholecystitis. Ultrasonography may yield a diagnosis in a few minutes, while scintigraphy may require two to four hours. Because most patients with right upper quadrant pain do not have acute cholecystitis, the additional anatomic detail of other abdominal organs yielded by ultrasonography may be important.

Pancreas

Ultrasonography can satisfactorily demonstrate the pancreas in 85% to 90% of individuals and can be primarily used for diagnosing the condition of the patient with pancreatitis or the patient suspected of having pancreatic neoplasm.[28,29] If diagnosis of the condition of a patient with acute pancreatitis is needed, ultrasonography is most useful if inflammation is mild or moderate. With mild pancreatic inflammation, the pancreas may appear normal or may be enlarged and hypoechoic secondary to edema. Because of its sensitivity in detection of gallstones, ultrasonography is useful for gallbladder evaluation if gallstone pancreatitis is suspected.[29]

In the severely ill patient with pancreatitis, computed tomography will identify more extrapancreatic fluid collections than ultrasonography and can give a more accurate evaluation of the amount of tissue necrosis.[29,30] The presence of gas and degree of hemorrhage are also better estimated with computed tomography.[30] If infection of a fluid collection is suspected, ultrasonography- or computed tomography-guided aspiration can safely be performed.

Chronic pancreatitis presents imaging difficulty. Ultrasonography may demonstrate diffusely increased echoes because of fibrosis and calcifications; however, computed tomography and ultrasonography examinations will often be normal and cannot be used to rule out the diagnosis.[31] Focal pancreatic enlargement of focal masses different in echo texture from the remainder of the pancreas may be seen, and guided biopsy studies of suspicious masses may be necessary.[31] While present only in the minority of cases, small pancreatic calculi may be visualized on ultrasonography and computed tomography when not seen on conventional roentgenograms. Ultrasonography can demonstrate normal or enlarged pancreatic ducts, but usually only portions of the ductal system are seen.[32] Therefore, endoscopic retrograde pancreatography remains the procedure of choice for evaluating the pancreatic ductal system and for grading the degree of pancreatic parenchymal damage.

Ultrasonography is valuable in the search for pancreatic tumors. The sensitivity of tumor visualization is related to the diligence of the sonologist. In a recent series where ultrasonography was used as the initial screening method, 50 (98%) of the 51 pancreatic malignant neoplasms were visualized.[33] In many comparative series, computed tomography sensitivity and specificity for pancreatic cancer detection are greater and more consistent than those for ultrasonography.[34] If computed tomography is used for initial screening, ultrasonography is especially accurate in differentiating tumor from normal pancreas when directed to an area questionably abnormal on computed tomography images.

Ultrasonography may understage pancreatic cancer by failing to detect abnormal regional lymph nodes. Given the high likelihood of finding unresectable tumor at the time of surgery in these patients, great care must be used in staging. Multiple imaging studies including ultrasonography, computed tomography, cholangiography, pancreatography, and often angiography are needed.

Ultrasonography is especially useful for detection of pancreatic insulinomas and may demonstrate these small lesions preoperatively in more than 60% of patients.[35] Ultrasonography sensitivity is especially high at surgery, when unpalpable lesions can be found when the ultrasound transducer is placed directly on the exposed pancreas.[35]

Spleen

The spleen is often difficult to completely visualize with ultrasonography because of its subcostal, retrogastric location. With diligence, splenic size and internal architecture can often be evaluated. When the spleen can be well visualized, ultrasonography is as sensitive as computed tomography for focal lesion detection.[36] Splenic cysts and abscesses can be identified and focal and diffuse solid masses can be seen.[36] Clinical history and aspiration or biopsy are often necessary for specific characterization when focal splenic disease is visualized.

Ultrasonography can be useful for the examination of patients suspected of having acute splenic infarction, but chronic infarction poses a sonographic challenge because of a wide spectrum of ultrasonography appearances. Computed tomography is a more common choice in the evaluation of splenic trauma, in part because computed tomography is more accurate for splenic injury demonstration. If splenic trauma is conservatively managed, ultrasonography is an effective method of following up a hematoma to resolution or of searching for splenic abscess formation.

Abdominal and Retroperitoneal Adenopathy

Many early studies comparing ultrasonography and computed tomography in the detection of adenopathy demonstrated that the former was of value in nodal detection; results were similar to those obtained with computed tomography. Retroperitoneal and abdominal nodes can be detected, but the detection of adenopathy by ultrasonography is technically difficult, and there is greater variability in interpretation than with computed tomography.[37] The exquisite retroperitoneal detail and ease of computed tomography examination have made computed tomography the more popular examination for nodal detection.

Abdominal Aorta

Ultrasonography is the procedure of choice for screening and follow-up of the patient with suspected abdominal aortic aneurysm. Ultrasonography is an accurate tool for aorta measurement because the ultrasonography transducer can be angled or rotated perpendicular to the lumen of the vessel despite prominent lumbar lordosis or aortic tortuosity. In many patients, ultrasonography can define the superior extent of the aneurysm relative to the kidneys and extension into the iliac arteries.[38] However, if the aorta is obscured by overlying gas, especially in the massively obese patient, computed tomography evaluation is necessary.

Ultrasonography is of less value in diagnosing the condition of the patient with acute aortic disease. In a recent study, an ultrasonography machine was immediately taken to a triage room on ambulance radio notification of incoming patients suspected of having abdominal aortic rupture. Ultrasonography was 98% accurate in aneurysm detection, but only 4% sensitive for the detection of leakage.[39] This suggests that ultrasonography has no place in the emergency evaluation of the patient with a known aneurysm if leakage is clinically suspected. Since computed tomography is sensitive for this diagnosis, it is recommended if the patient is stable and the diagnosis in doubt.

Inferior Vena Cava

While the inferior portion of the inferior vena cava is often obscured by bowel gas, ultrasonography can rapidly and accurately evaluate the superior portion of the inferior vena cava without need for computed tomography or contrast cavography.[40] Inferior vena cava examination is necessary in patients with potential caval tumor extension because a caval mass radically alters the prognosis or surgical management of neoplasms. Extension into the inferior vena cava occurs most commonly with renal, adrenal, or hepatocellular carcinoma. If inferior vena cava obstruction is suspected, ultrasonography can often identify the cause and/or level.[40] Ultrasonography is also of value for localization of inferior vena cava filters. Flow above and below the level of such a filter can be noninvasively and accurately evaluated with Doppler studies.

Adrenal Glands

The technique of adrenal ultrasonography has been well described and, with diligence, high accuracy can be attained.[41] Other researchers point out the difficulty of imaging small lesions, inadequate imaging of the left adrenal gland, and the occurrence of false-positive rates as high as 39%.[42] Because computed tomography can visualize almost all adrenal glands and is more accurate in lesion detection, computed tomography has become the primary imaging choice.

Kidneys, Ureters, and Urinary Bladder

Ultrasonography is sensitive for the detection of renal failure secondary to obstruction since almost all patients with obstructive uropathy demonstrate anatomic dilatation. For this reason, a normal renal ultrasound examination virtually excludes the possibility of obstruction as a cause of renal failure.[43] However, dilatation is a nonspecific finding, and obstruction, vesicoureteral reflux, relieved obstruction, high urine flow states, and postsurgical and congenital changes can yield a similar appearance. Therefore, if dilatation is identified on ultrasonography, more specific imaging such as technetium 99m-pentetic acid scintigraphy with or without furosemide, antegrade pyelography, or retrograde pyelography is necessary. If obstruction is present and drainage for function preservation or infection is necessary, ultrasonography guidance for percutaneous nephrostomy tube drainage is often indispensable.

Caution must be used when interpreting the ultrasonic images of a patient with acute obstruction because little, if any, dilatation may be present, and nuclear imaging or contrast visualization may be needed.

While ultrasonography may confirm the scarred, small kidneys of the patient with chronic renal cortical disease, it is insensitive if renal cortical disease is early or mild. Although there is a direct relationship between renal cortical echogenicity and glomerular interstitial histologic change, with the single exception of polycystic disease ultrasonography remains unable to categorize specific types of cortical disease.[44]

Ultrasonography can confirm the common diagnosis of simple renal cyst and localize solid renal masses. There are, however, few ultrasonography clues to neoplasm characterization. Angiomyolipoma is the exception, with uniform, dense echoes suggesting the fibrofatty tissue that may be present. If true fat can be confirmed on computed tomography, diagnosis is certain.[45]

Ultrasonography should not be used as the sole means of excluding malignant neoplasms of the urinary tract. Small urothelial tumors within the kidney are difficult or impossible to visualize, and cortical neoplasms smaller than 2 cm are often of the same echo texture as the renal cortex.[46] Therefore, intravenous urography remains the best primary means of urinary tract examination of the patient with hematuria.

Ultrasonography is useful for evaluation of a nonfunctioning kidney or intravenous urography and can rapidly help to differentiate obstruction from vascular occlusion.

Ultrasonography is sensitive for the detection of calculi in the kidneys,[47] but bright, shadowing echoes can also be caused by calcified sloughed renal papillae, calcified tumors, and vascular calcifications.

The ureters are not usually well seen with ultrasonography, except for their proximal and most distal portions. Ultrasonography may be helpful in these areas to confirm the presence of dilatation, filling defect, or mass.

Although ultrasonography may demonstrate urinary bladder malignant neoplasms, the combination of intravenous urography and cystoscopy is most often used if bladder cancer is suspected since urography is able to evaluate the upper tracts, and the cystoscope can help find and complete biopsy studies of smaller tumors. Bladder diverticula and stones can be demonstrated with ultrasonography, and postvoid bladder residuals can easily be determined without the need for Foley catheter placement.[48]

Sonography has become important in the postoperative evaluation of renal transplants because of its sensitivity in detection of renal obstruction, fluid collections (seroma, hematoma, urinoma, and lymphocele), and major vascular complications.[49]

Prostate

The most significant characteristic of transrectal ultrasonography of the prostate is that an imaging modality now exists that can safely identify lesions of prostate cancer not clinically palpable.[50] However, the sensitivity and specificity of ultrasonography for detection of prostate cancer are difficult to determine because biopsies of most ultrasonographically normal prostates are not performed, and patients with ostensibly benign disease do not undergo the same treatment as patients suspected of having cancer. It remains to be demonstrated that ultrasonography screening leads to improved patient survival at an affordable cost.[51,52] It is too early to endorse ultrasonography as a screening tool for prostate cancer.[53]

Few data are available to suggest that transrectal ultrasonography guidance is mandatory for biopsy studies of a palpable prostatic nodule. If only questionable induration of the prostate is present or if an abnormality has been found only on transrectal ultrasonography, then ultrasonography may be useful in directing a needle to the area in question.

When a tissue diagnosis of prostate cancer has either been made by biopsy or is incidentally found at transurethral resection for ostensibly benign disease, transrectal ultrasonography may be specific for evaluation of potential macroscopic capsular and seminal vesicle invasion.[54] However, since computed tomography and MRI may demonstrate abnormal pelvic lymph nodes not visible on transrectal ultrasonography, these studies are still helpful for presurgical evaluation.[55,56]

Transrectal ultrasonography can be used to accurately place radioactive seeds for therapy of prostate cancer and can accurately define ports for external beam irradiation. After radiation or hormonal therapy, transrectal ultrasonography can monitor the change in size of a known prostatic cancer lesion.

Transrectal ultrasonography is accurate in estimation of volume of hyperplastic prostatic tissue and can identify and guide drainage of prostatic abscess. Preliminary results demonstrate that transrectal ultrasonography may be useful in the diagnosis of voiding difficulties and can provide information not easily obtained by cystoscopy or cystogram.

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Fairfield County Medical Association's Executive Director to Retire

The Fairfield County Medical Association's Board of Trustees has announced the retirement of its Executive Director, Leonard R. Tomat, effective August 31, 1991.

In his fifteen years of service, Mr. Tomat coordinated the activities of the 1800-physician organization. As Executive Director he was responsible for planning special events, editing publications, responding to media and public inquiries, and addressing legislative issues. Of all his accomplishments, he considers the success of FCMA's peer review mechanisms among the finest of any available. The reviews included situations involving the cost utilization and quality of medical services. Mr. Tomat is equally proud of the communications which the Association has established with its physician members. The Association's members look to the FCMA staff as a reliable source for timely information on the issues facing medicine.

Before coming to The Fairfield County Medical Association, Mr. Tomat was the Assistant Executive Director for Educational Activities for the Connecticut State Medical Society for seven years. In this capacity, he developed the accreditation program for continuing medical education at the thirty-six Connecticut community hospitals and implemented the Society's first endorsed professional liability program, including loss control, claims review and legislative reform.

Prior to joining CSMS, Mr. Tomat was the Associate Director of External Affairs for Trinity College in Hartford. In his ten years at Trinity College, he was also the Assistant Dean of Students and Director of the Mather Student Center.

A native of Vermont, Mr. Tomat began his career teaching English and speech at Montpelier High School in Montpelier, Vermont. He continued his teaching career at Riverdale County School for Boys in New York City where he was also the school's Director of Student Activities. A graduate of the University of Vermont, Mr. Tomat received a Master's Degree from New York University.

Mr. and Mrs. Tomat will make their permanent residence in South Orleans on Cape Cod.

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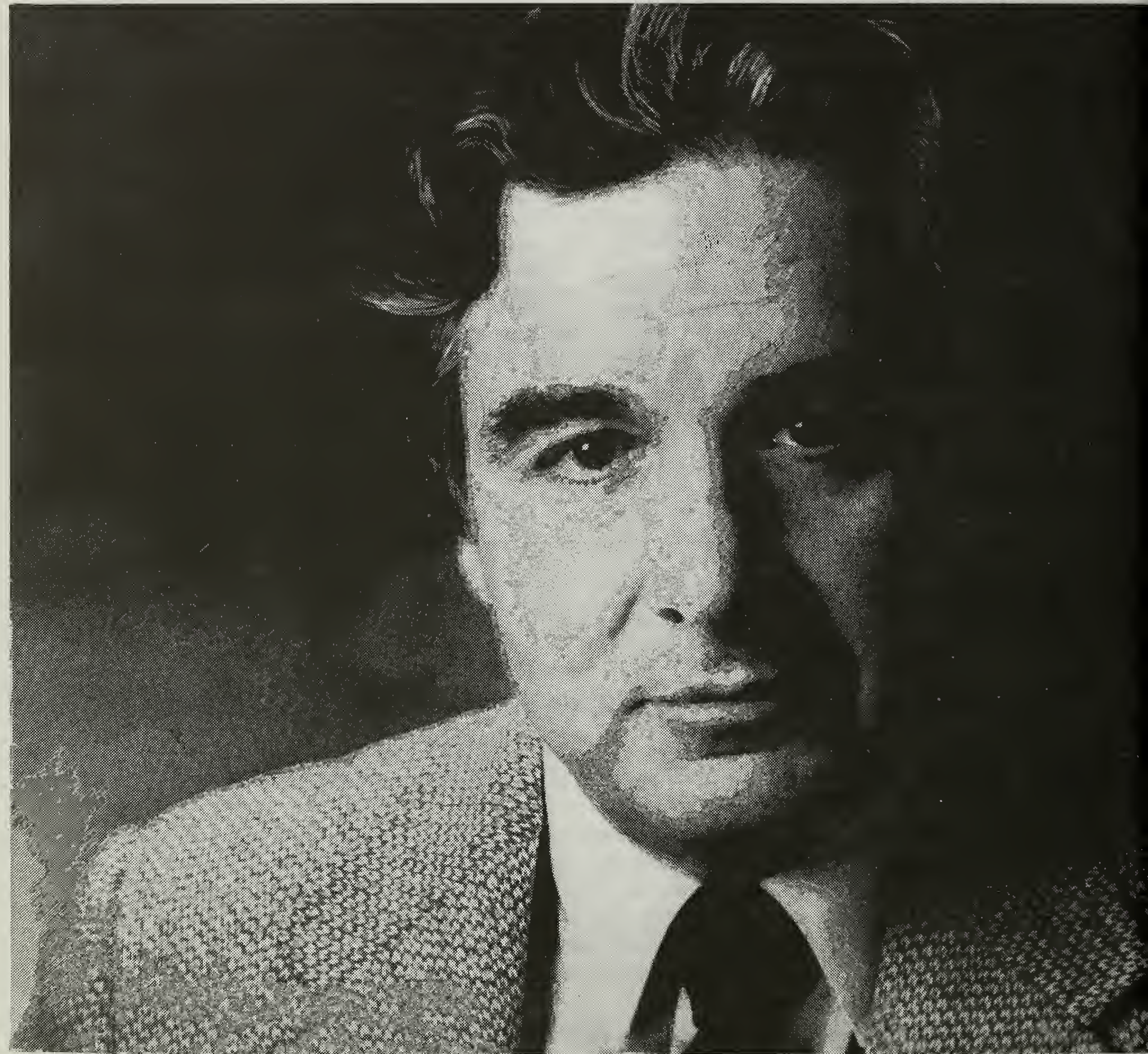
—Dr. Vincent Catrini, General Surgery, Middletown, CT



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Various Thoughts

E. TREMAIN BRADLEY, M.D.

IT seems that once I've said my piece, there's often something else I wish I had said. For instance, with a wound open and clamps on bleeders inside, ligatures need to be applied, without tearing the fragile vessels. Two things help. First, as the tie is passed around the point of the clamp, a little hook can be made in the vessel by easing the clamp inward a little. This prevents the ligature from slipping off or riding up onto the clamp. Then, when the knot is set, one end of the ligature is held outside the wound *without tension*, while the other end is pushed down deep, beyond the vessel. Thus no drag is placed on the ligature or the vessel during tying, nor should there be while the tie is being cut. Also, we must beware of a clamp lying against the edge of a wound lest pressure on the handle cause leverage that tears it loose from its captive below.

When removing an appendix, the cecum is often protected from contamination by gauze. If the gauze is cut to surround the appendix, little pieces of thread are apt to fall out, remaining as foreign bodies. Using an abdominal pad or just folding a piece of gauze will avoid this; likewise if gauze is being used as a drain.

The femoral artery having been palpated and the skin incision made over the saphenous vein, I prefer no further cutting, but merely spreading the soft tissues to disturb the lymphatics as little as possible—to diminish lymphorrhea.

Wiping the preservative off the catgut with a blood-soaked sponge or even just saline-soaked may reduce inflammation. Skin sutures in the groin should be very loose to minimize maceration and infection. When varicose veins have been removed and elastic bandages applied for compression, I stabilize the dressings by running one-inch adhesive from the skin just above the bandage, down under the arch of the foot and up the opposite side to the skin.

Wounds do well when dressings are changed no more often than necessary and if dry even left open to the air.

Approximation of the edges of a round, elliptical or pear-shaped wound results in a bunch at the end: a "dog ear." An easy way to revise this, once the edges are brought close with skin hooks, sutures, or towel clips, is to place a towel clip at the apex of the dog ear and lift enough to match the skin tension at the edges. Then a V is cut extending the two arms along the base on each side to meet the approximated skin edges.

As the surgeon runs a continuous suture, the line is most efficiently held between thumb and index finger with slight tension toward the open end of the wound, but in such position that it is readily pulled loose when the surgeon pulls through his next stitch. The suture is then grasped again in the same manner.

After skin closure with interrupted sutures, they can all be held together with minimal tension, allowing the fingers to slip up slightly after each one is cut. This lifts the cut threads up out of the way for the next to be cut.

Jerk Protection: When working around the eyes, ears and face, I believe in having the hand which holds the instrument touch the head and in such a way that if there should be sudden movement, the instrument will pull away from the patient rather then plunge into an undesirable spot. This is a particularly important precaution when procedures are being done under local.

E. TREMAIN BRADLEY, M.D., solo practice of General Surgery, retired to Norfolk, Conn.

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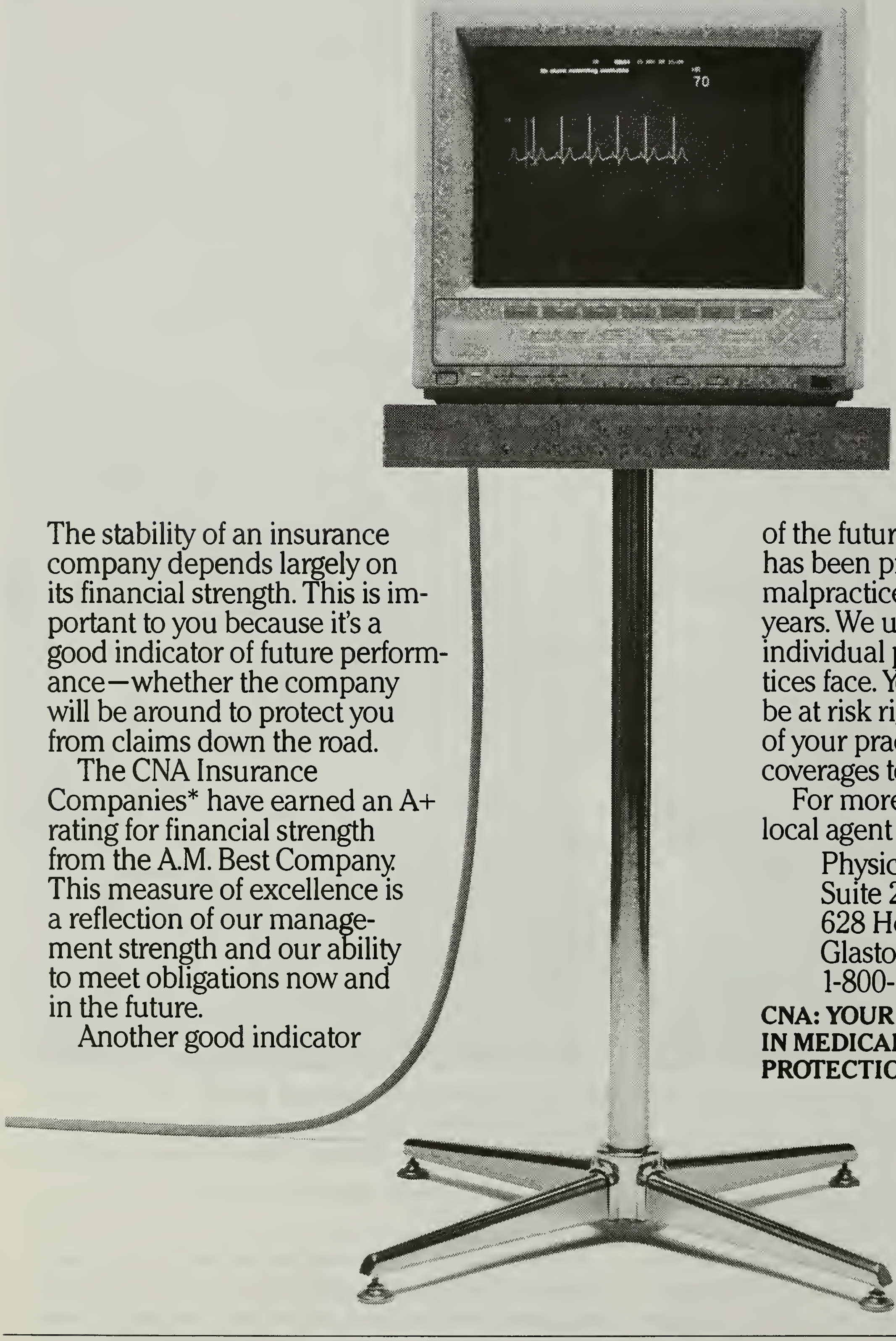

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Editorial

Guest Editorial

Overturn the Gag Rule

In its eagerness to suppress abortion counseling, the Supreme Court has opened the way for censorship in all programs and institutions receiving federal funds. It should be soundly condemned.

In *Rust v Sullivan*, the Court held constitutional a government regulation prohibiting abortion counseling and referral by those working in clinics that receive Title X funds. This is censorship of professional speech. But by redefining "speech" as "activity" when it comes from a doctor employed by such a clinic, a five-four majority of the Court endorsed the censorship.

Under the regulations upheld by the court on 23 May, a doctor in a Title X clinic may not discuss abortion with a pregnant client. Even if the patient requests information about abortion, the doctor must reply (as dictated by the Regulations), "This project does not consider abortion an acceptable method of family planning." A pregnant client must be referred for prenatal care.

In addressing the infringement on the doctor-patient relationship, the Court sanctioned two types of medical advice, one for private patients and one for clinic patients:

> Nothing in the Regulations requires a doctor to represent as his own any opinion that he does not in fact hold. Nor is the doctor-patient relationship established by the Title X program sufficiently all-encompassing so as to justify an expectation on the part of the patient of comprehensive medical advice. The program does not provide post-conception medical care, and therefore a doctor's silence with regard to abortion cannot reasonably be thought to mislead a client into thinking that the doctor does not consider abortion an appropriate option for her.

The Court apparently assumes that each clinic patient has a private doctor who can give her the "comprehensive medical advice" that the Title X doctor must withhold. The Court also ignores that the regulations do not permit the doctor to be silent, but compel that statement, "This project does not consider abortion an acceptable method of family planning" and further compel referral for prenatal care.

Justice Blackmun expressed outrage at the majority's analysis. "It cannot seriously be disputed that the counseling and referral provisions at issue...constitute content-based regulation of speech. Title X grantees may provide counseling and referral regarding any of a wide range of family planning and other topics, save abortion." He noted that the Regulations are also viewpoint-based. They suppress speech "favorable to abortion with the one hand" and compel anti-abortion speech with the other." He wrote:

> The Court, for the first time, upholds viewpoint-based suppression of speech solely because it is imposed on those dependent upon the Government for economic support. Under essentially the same rationale, the majority upholds direct regulation of dialogue between a pregnant woman and her physician when that regulation has both the purpose and effect of manipulating her decision as to the continuance of her pregnancy...Until today, the Court never has upheld viewpoint-based suppression of speech simply because that suppression was a condition upon the acceptance of public funds. Whatever may be the Government's power to condition the receipt of its largess upon the relinquishment of constitutional rights, it surely does not extend to a condition that suppresses the recipient's cherished freedom of speech based solely upon the content or viewpoint of that speech.

But Justice Blackmun was in the minority.

Unless Congress repudiates the Court and reauthorizes Title X without the "Gag Rule," the *Rust* decision will have a devastating impact on the network of 4,000 Title X clinics which have provided reproductive health care for tens of thousands of poor women since 1970. But the message of *Rust* about the majority's willingness to tolerate government intrusion into the doctor-patient relationship and censorship of professional speech is even more frightening.

The Court reasoned that the government can, "without violating the Constitution, selectively fund a program to encourage certain activities it believes to be in the public interest, without at the same time funding an alternative program which seeks to deal with the problem in another way. In so doing, the Government has not discriminated on the basis of viewpoint; it has merely chosen to fund one activity to the exclusion of another." The implications and potentially broad application of this funding analysis represent a substantial threat to the effective practice of medicine. For example, the rationale could support a regulation requiring doctors working in Veteran's Administration hospitals to withhold advice regarding post-traumatic stress syndrome, even if that were the reason for which the patient was seeking treatment. The doctor could be required to refer such a patient to physical therapy. If the patient asked specifically for psychotherapy, the doctor could be required by regulation to say, "This hospital does not consider psychotherapy to be an appropriate treatment for post-traumatic stress syndrome." In condoning the manipulation of doctor-patient speech, the Court has sanctioned the dictation of medical practice.

Because the Supreme Court's decision in *Rust v Sullivan* conditions the receipt of federal funds on the curtailment of speech, it potentially affects all those receiving not just Title X funds and veteran's benefits, but those receiving Medicare, Medicaid, Title XX or government research funds as well. It could even justify the censorship of speech of teachers in schools with federally-supported lunch programs and perhaps employees of states which receive federal highway funds.

Write your representative in Congress. Thank them for their support of the reauthorization of Title X without the Gag Rule. Write your colleagues in other states and get them to write their congressional representatives.

Penelope I. Bellamy

PENELOPE I. BELLAMY, President of the Board of Planned Parenthood of Connecticut. She is an attorney with Wiggin and Dana in New Haven.

Freedom of Communication Between Physicians and Patients

Resolution Adopted by the American Medical Association

RESOLVED, That the American Medical Association strongly condemns any interference by the government or other third parties that causes a physician to compromise his or her medical judgment as to what information or treatment is in the best interest of the patient; and be it further

RESOLVED, That the American Medical Association working with other organizations as appropriate, vigorously pursue legislative relief from regulations or statutes that: (1) prevent physicians from freely discussing with or providing information to patients about medical care and procedures; or (2) interferes with the physician-patient relationship; and be it further

RESOLVED, That the American Medical Association communicate to the Department of Health and Human Services its continued opposition to any regulation that proposes restrictions on physician-patient communications; and be it further

RESOLVED, That the American Medical Association inform the American public as to the dangers inherent in regulations or statutes restricting communication between physicians and their patients.

50 Years Ago

From the *Journal of the Connecticut State Medical Society*

August 1941

Quo Vadis?

"To-morrow, and to-morrow, and to-morrow,
Creeps in this petty pace from day to day
To the last syllable of recorded time,
And all our yesterdays have lighted fools
The way to dusty death."*

In the light of the present world aflame and in war torn anguish these words of the poet become prophetic. The past quarter century has known fully the bitter dregs of war and its aftermath and succeeding to-morrows will undoubtedly be no less palatable. Nevertheless, in reviewing the five years 1936-1941 since the *Journal* has been fulfilling its mission of purveyor of information to the Connecticut State Medical Society, there have been put in motion beneficient forces which have had unprecedented influence on the national and individual life.

Consider, if you will, some of the steps which have lifted our Society from what might easily have been an isolation of smugness and self satisfaction to its present position of progress. Prepaid hospital insurance has become a reality and, due to the keen insight of our Council, an asset to medical practice. Careful study of the possibilities of prepaid medical service is being made by our committee. A Public Relations Committee with a speakers' bureau has been developed. At present compulsory health—or sickness—insurance is not in force, but we are wide awake to that eventuality and are at all times ready to discuss with Labor and Capital any program which shall offer better quality rather than quantity of medical care. Invaluable to our Society has been the appointment of a full time Executive Secretary whose familiarity with the events in Washington and Chicago has been no less than in our own capital.

The membership of the Society has increased from 1580 to 1825, notwithstanding loss by many deaths and in spite of the increased financial tax. We shall need this increase in numbers to meet the challenge hurled at us by the vital need of medical preparedness. The fact that already plans have been put in motion to this end during the past year may be news to some, or may have been casually brushed aside for the moment. Indifference to the forces of the current will be disastrous to the physician, be he isolationist or strong for all out aid to Britain. That the armed men of this country will increasingly require medical aid is self evident. Industry and its attendant housing problems is another phase of defense requiring medical assistance.

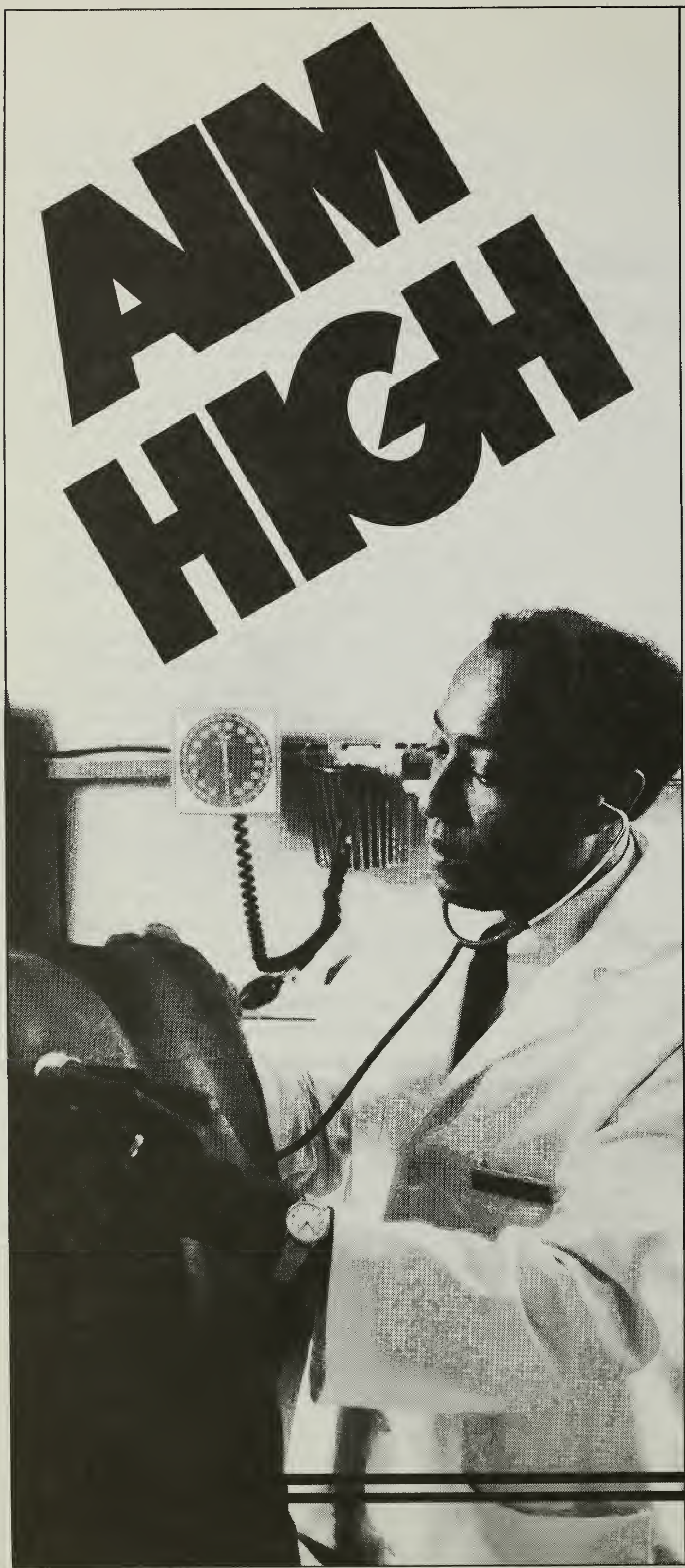
With the swift moving events of these uncertain days there can be no assurance that the practice of medicine will remain unchanged. Every American physician will be called upon to take his part in the effort to preserve the American way of life and to redouble his zeal in contributing the best at his command to his chosen profession.

"I do not know beneath what sky
Nor on what seas shall be thy fate;
I only know it shall be high,
I only know it shall be great."**

* Shakespeare; Macbeth, Act V, Sc. V.

** Richard Hovey: Manifest Destiny

—Editorial from *The Connecticut State Medical Journal*, August 1941.



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AIR FORCE

England's National Health Service: 43 Years Later

As a product of a London medical school who has practiced here for over 30 years, but has maintained close ties with my graduating class, I feel it is appropriate to bring you all up to date as to what has happened to the National Health Service in England. This is especially interesting in view of the fact that similar noises are currently being made in America by business, the insurance industry and government. England now has a two-tiered system with excellent basic medical care for all, and a free-choice service for those who want it and can afford to pay for it.

The "National Insurance Scheme" was started 80 years ago and it provided compulsory coverage for every working person in Great Britain, and it was paid for by a wage tax similar to Social Security. In 1948 this plan was extended to all who lived in the United Kingdom. There were and are two parts of the National Health Service—the Hospital Service which immediately acquired all the hospitals and consulting staffs, and the General Practitioner Service.

The latter is a strict gatekeeper service which is the first point of ALL medical contact for the patient. The only exception is the emergency room, but even here, if the emergency room physician feels the patient can wait, he is sent home to await an evaluation by his general practitioner. Letters of referral are the only means of obtaining a consultation with a specialist. Consultations are all done in the hospital in a clinic setting. The hospital annual budget decides the speed of the consultation and any necessary hospitalization and/or surgery. As funds run low at the end of the year, beds and operating rooms are closed and the waiting lists lengthen.

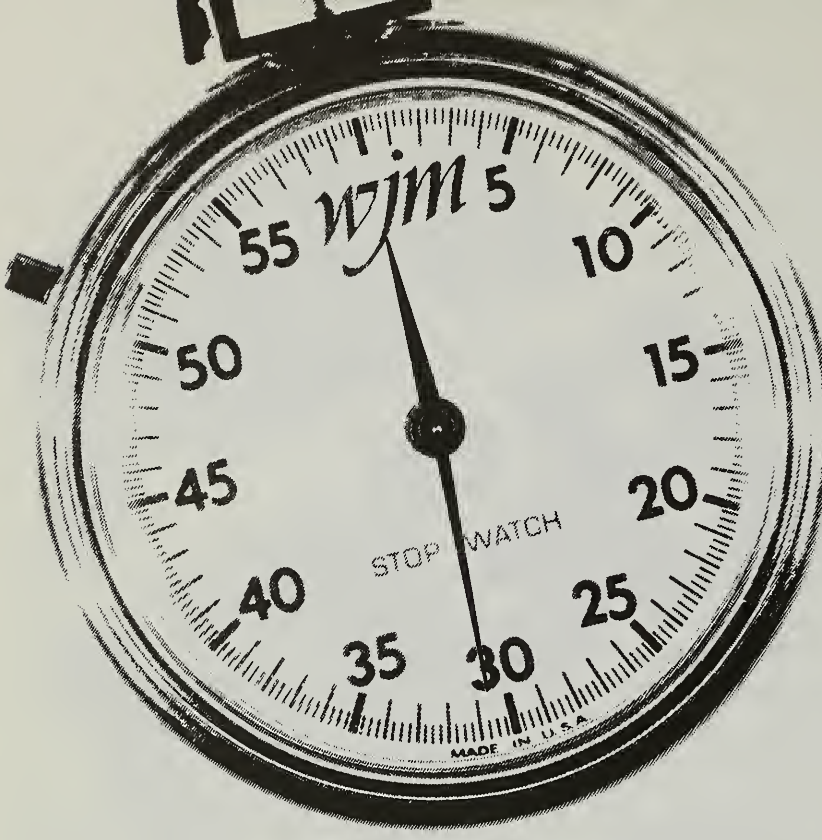
All consultants are paid the same, be they neurosurgeons, orthopedists or internists. A good general practitioner's salary is equal to a consultant's. Ever since World War II, and maybe even before, queuing has been a way of life for the average English person, so to wait for a month or two to see a consultant, and another month or year for surgery is very acceptable.

However, 25% of the population have opted for a speedier level of care. Thus has been introduced into England the second tier of medical care. This is currently in place throughout the country, although London, with all the major medical schools, has the highest number of, shall we say, "private patients."

Those in both levels use the General Practitioner Service, but when anything goes wrong, the 25% in the upper level immediately get treated using an insurance plan or the equivalent. Consultants who wish to supplement their National Health Service salaries moonlight in Harley and Wimpole streets, and have built new and modern private hospitals mainly with Arabian money. The number of private beds is quite limited, but the ever-inventive French have started to open hospitals along their northern shores, so that the English no longer have to wait two to three years for cataract surgery and hip replacement.

The system has come a long way and a two-tiered system seems to be working well in England. Certainly the people of Great Britain think it's a good system. A two-tiered system may seem un-American, but if you think about it, nearly everything else we do in life is tiered—all housing, cars, and clothing vary from person to person, depending on financial outlays. Maybe such a system might work here, although I feel fairly certain that at least 75% of our population would likely plan on using the "upper tier."

Anthony P. Redmond, M.D.
President



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REFLECTIONS ON MEDICINE

An Unrestrained Spending Spree

ROBERT U. MASSEY, M.D.

ANYONE with a passing knowledge of history knows that all complex human institutions finally fail. Potential dissolution is built into the fabric of things; it is the second law of thermodynamics paralleled in human affairs, time's arrow. But we grow up regarding some institutions as "solid as the Rock of Gibraltar": banks, insurance companies, great corporations, fine old department stores. When they go down we feel a shiver of momentary terror that the fabric may be unraveling. Those old enough to remember the Great Depression recall the bank closings in 1933, but that was a singularity, never to happen again, and anyway the closings were temporary; First National came back.

Last month the state government seemed on the verge of dissolution, although we knew it would pull through. But banks and insurance companies have failed, and financial institutions have gone under in dishonor. In Europe, great nations are disintegrating, and some speak of the end of the nation-state as we have conceived it. We feel secure because our nation, like a healthy organism, has built-in strategies to maintain the *milieu interieur*: a Constitution of checks and balances and a market economy controlled quite involuntarily by the invisible hand. What happens if those should fail to work? Central planning, as we suspected all along, has been shown a failure, and our version of it, bureaucratic regulation, has been powerless to keep financial institutions from disaster.

Are health care costs about to do us in? When they accounted for 9% of the GNP some of us asked, "What's bad about that? Maybe that's a sign of enlightenment." But in our uneasiness we agreed this creeping growth must stop somewhere, maybe at 12%. It is now there and since 1977 has been increasing at the rate of 3% annually *in real terms*. From 5.5% in 1965, it is expected to reach 15% of the GNP by the year 2000.[1] The hope has been that the market would finally pull in the reins, and perhaps it will, but health insurance premiums increased by more than 17% between 1989 and 1990, most of this borne by employers who now pay about 6% of their payroll expenses for health benefits—up from 2% in 1965.[2] None of this affects the health care market; these costs are lost in the increasing costs of goods and services. Who among us makes the connection, and who will decide to use fewer health services because they cost too much? Few, besides the employer, feel the pinch of these increasing costs. Insurance companies simply raise their rates; hospitals, health care unions, doctors and nurses, pharmaceutical houses, surgical supply companies, all those that benefit from an enterprise employing 8.4 million workers will hardly devote themselves wholeheartedly to controlling health care costs.

Where then is the discipline, where the market forces to stabilize these costs at 12%, or better, reverse them? Capping real expenditures at, say, the rate of growth of the GNP is a suggestion easily made, but that is wage and price control and has never worked except in the short term. In Connecticut the hospital commission might hold hospital charges to the rate of inflation, but there would always be convincing reasons to make exceptions. The federal government might hold the line on Medicaid and Medicare payments—no more money—but then the pressure is on the states to come up with the difference. Something like that is happening in Canada now, and the squeeze is on the provinces. Recent events have shown the folly of depending on politicians to face unpopular issues.

Only the individual, by making choices, can restrain the market. Only when he decides to spend $100 to take the family out to dinner rather then $150 for an annual physical does the market work. But what if he makes decisions that adversely affect his family or the community? What if he opts for dinner out rather than for care of his wife's diabetes? Well, some would say, in a free society, he has that choice; others that society has an obligation to provide for the public welfare. Surely any solutions must encompass both societal interests and individual choice, but any scheme for payment that does not cost the individual enough to deny him the means to some other good that he wants will not stop the pernicious growth in health care expenditures. A 3% yearly unrestrained growth *in real terms* in anything—population, malignant cells, or health care costs—must finally wreck the system.

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2. Levit KR, Freeland MS, Waldo DR: National health care spending trends: 1988. *Health Aff* 1990; 9(2): 171-84.

ROBERT U. MASSEY, M.D., Professor, Division of Humanistic Studies in Medicine, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

LAW, MEDICINE, AND PUBLIC POLICY

The *Moore* Case and the Doctor Patient Relationship

JOSEPH M. HEALEY, J.D.

WHILE most of the attention of commentators discussing the *Moore* case[1] has focussed on issues of possession and ownership of human cells, tissues, and organs, there is a second aspect of the case which should not be overlooked. In holding that John Moore was entitled to bring a legal action for the unauthorized performance of medical procedures, the California Supreme Court[2] relied upon two alternative legal theories to support this conclusion. The first is the doctrine of informed consent. This is a familiar concept to health professionals and involves an area of health law in which there has been a great deal of activity during the past twenty years. The doctrine of informed consent imposes a duty upon physicians to provide sufficient information to permit patients to exercise their right of self-determination. In the *Moore* case, failure to provide Mr. Moore with sufficient information about the potential use of his cells might serve as a breach of his duty, actionable under California law.

The second theory is the doctrine of fiduciary relationships. This doctrine is less familiar to health professionals and involves an area of health law that is much less well developed and much less well understood. The acknowledgment that the doctor-patient relationship is a fiduciary relationship would result in the application of higher standards in some aspects of the relationship than those ordinarily imposed by the law of contracts or the law of torts. Examples of individuals held to such higher standards in other relationships include agents, partners, directors, officers, trustees, executors, administrators, bailees, and guardians.[3] The *Moore* case raises two questions in this regard: (1) Should the doctor-patient relationship be treated as a fiduciary relationship? and (2) What would be the implications of such a characterization?

Though it is often assumed that the relationship between doctor and patient is a fiduciary relationship, this assumption has not always been fully explained or justified. In recognizing the concept of fiduciary relationships the law acknowledges that there are some relationships involving a special trust within which, as a matter of public policy, society is willing to impose higher, more protective standards to assure that the rights of the vulnerable party are not abused by the more powerful party. Those who argue that the doctor-patient relationship should be considered a fiduciary relationship emphasize the destructive impact of illness, disease, and injury upon the patient's ability to function and the importance of trust to support the patient's expectation that the doctor will exercise independent clinical judgment for the patient's well-being. Though usually able to retain the right to make decisions about their own health care, patients are nonetheless exposed to the possibility of harm because of their vulnerability and because of the imbalance of power between them and their physicians. In this sense, the doctor-patient relationship resembles the other types of relationships subject to the higher standards imposed upon fiduciary relationships and deserves to be treated as one itself.

This was acknowledged in the *Moore* case, when the California Court concluded:

> Accordingly, we hold that a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment.[2]

Note, however, that the Court limited the application of the concept of a fiduciary relationship:

> In some respects the term "fiduciary" is too broad. In this context the term "fiduciary" signifies only that a physician must disclose all facts material to the patient's decision. A physician is not the patient's financial adviser. As we have already discussed, the reason why a physician must disclose possible conflicts is not because he has a duty to protect his patient's financial interests, but because certain personal interests may affect profession judgment.[2]

The implications of the *Moore* case for the duty to disclose will be examined in next month's concluding column on the *Moore* case.

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3. See Frankel T: Fiduciary law. 71 Cal. L. Rev. 795 (1983).

JOSEPH M. HEALEY, J.D., Associate Professor, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington, CT.

MEDICAL NEWS CAPSULES

This Month's Reading in Review

TIMOTHY B. NORBECK

- It should be remembered that the recent "soft" insurance market now producing some stability in medical liability premiums is by no means a permanent phenomenon...The severity of claims, as well as costs of defense, continue to increase...AMA's most recent survey data indicates that claims frequency increased in 1989 for the first time since 1985...The insurance crisis periods in both the early 1970s and 1980s were preceded by times of relative calm.
- *"The representatives of the people, in a popular assembly, seem sometimes to fancy that they are the people themselves, and betray strong symptoms of impatience and disgust at the least sign of opposition from any other quarter."* ...So spoke Alexander Hamilton some 200 years ago...As skeptical of politicians as he was, even Hamilton would probably be shocked at the happenings in California now that the voters have created term limits for state legislators...As the *Wall Street Journal* explains, "The incumbents are so driven to keep their jobs that they have sued the people" in an effort to overturn proposition 140...Proposition 140, which imposed limits of two four-year terms on state senators and three two-year terms on state representatives, has been challenged in the courts in the name of the California legislature...As the *Journal* says, "The American rule that if you lose in politics, try the courts even applies to legislators!"
- According to a recent report by the Teen Pregnancy Prevention Coalition of Connecticut, the pregnancy rate for 10 to 14 year-olds rose 100 percent between 1980 and 1987...The rate for 15 to 19 year-olds increased by 23 percent.
- An interesting teen pregnancy program was conducted by the Johns Hopkins School of Medicine at two inner-city schools in Baltimore...Individual and group counseling, including medical and contraceptive services, were provided at two nearby clinics...Students at two other schools received only Maryland's required sex education courses...After three years, the pregnancy rate at the first two schools dropped by 30 percent while the rate at the other two schools increased by 58 percent.
- The U.S. General Accounting Office (GAO) estimates that 43 percent of total insurer defense costs are spent on claims that ultimately are closed in the defendant's favor...According to RAND Corporation studies, no more the 40 cents of every dollar spent in resolving medical claims ever reaches patients in the United States, making ours the most expensive claims resolution system in the world.
- While less than half of Medicaid expenditures go to people above poverty, almost 90 percent of Medicare expenditures go to people above the poverty level.
- Although families receiving Aid to Dependent Children constitute between 70 percent and 75 percent of the Medicaid population, three fourths of Medicaid expenditures go to the costs of care for the aged, blind, and disabled - especially patients in nursing homes.
- At 535, the U.S. Senate and House of Representatives have the same number of legislators as they did ten years ago...But the number of congressional employees has grown by 14,000 over that same period...Congress now employs 37,000 people, costing the taxpayers $3 billion a year...Personal staff working for individual members of Congress has tripled since 1960.
- The AFL-CIO is expected to endorse a presidential candidate by April of 1992...Organized labor wants a bigger role in choosing a candidate than it had in 1988...While there is no clear-cut favorite yet, either U.S. Senator Tom Harkin (D, IA) or New York Governor Mario Cuomo are likely choices.
- State legislators have killed a bill that would have been the first step toward rationing health-care services in Colorado...The legislation would have created a health-services commission charged with developing health-care priorities for the poor.
- *"I have come to the conclusion that I have let my integrity become restricted to the issues too much, and not enough, perhaps, to every act and procedure of my office"* ...So spoke U.S. Senator Mark Hatfield (OR) in confessing to the Portland *Oregonian* last month about gifts and free tuition for his son that were given to him by indicted University of South Carolina president, James Holderman..."Integrity restricters"?...As mentioned in *The New Republic*, "Has Hatfield revealed a new profession?...The possibilities for Washingtonians are virtually endless."
- As reported in *Business Week*, "How come many of our public servants, who grouse frequently about their meager paychecks, seem to be enjoying themselves so much"?...The answer seems to be wise use of Washington's many power perks: A members-only gym (with pool, weights, etc.) costs only $50 a year - The Capitol infirmary, where physicians provide no-charge laboratory, X-ray, and pharmaceutical services at a cost to the taxpayer of about $1.5 million a year - $5 for a Capitol barber shop haircut- $3 for a hand car wash at the Capitol garage - and a day-care center available for members and staff at low rates.

TIMOTHY B. NORBECK, Executive Director of The Connecticut State Medical Society.

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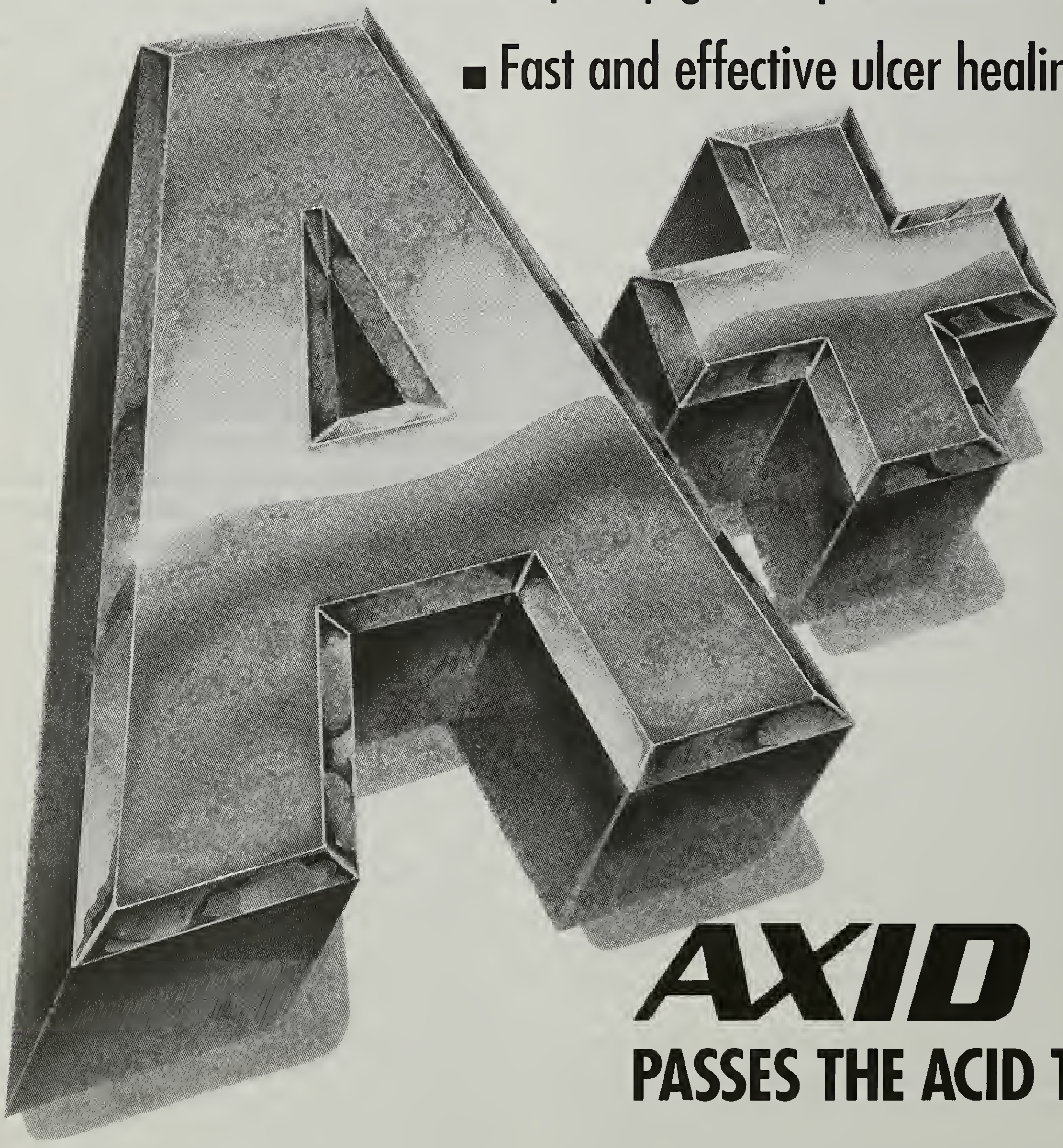

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*Most patients experience pain relief with the first dose.

See adjacent page for references and brief summary of prescribing information.

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Indications and Usage: 1. *Active duodenal ulcer*—for up to 8 weeks of treatment. Most patients heal within 4 weeks.

2. *Maintenance therapy*—for healed duodenal ulcer patients at a reduced dosage of 150 mg h.s. The consequences of therapy with Axid for longer than 1 year are not known.

Contraindications: Known hypersensitivity to the drug. Because cross sensitivity in this class of compounds has been observed, H_2-receptor antagonists, including Axid, should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists.

Precautions: *General*—1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests—False-positive tests for urobilinogen with Multistix® may occur during therapy.

Drug Interactions—No interactions have been observed with theophylline, chlordiazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility—A 2-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a 2-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a 2-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect; but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in 1 fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in 1 fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events were due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to 3 times the upper limit of normal, however, did not significantly differ from that in placebo patients. All abnormalities were reversible after discontinuation of Axid. Since market introduction, hepatitis and jaundice have been reported. Rare cases of cholestatic or mixed hepatocellular and cholestatic injury with jaundice have been reported with reversal of the abnormalities after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in 2 individuals administered Axid and in 3 untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H_2-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H_2-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis does not substantially increase clearance of nizatidine due to its large volume of distribution.

PV 2091 AMP
[091190]

References
1. Data on file, Lilly Research Laboratories.
2. *Scand J Gastroenterol.* 1987;22(suppl 136):61-70.
3. *Scand J Gastroenterol.* 1987;22(suppl 136):47-55.
4. *Am J Gastroenterol.* 1989;84:769-774

NZ-2943-B-149347

Additional information available to the profession on request.

Eli Lilly and Company
Indianapolis, Indiana
46285

Screening Mammograms and Pap Tests Medicare Coverage

TO ALL PHYSICIANS:

Medicare is now covering screening mammograms and Pap tests for older women. Below is information you can use to discuss this with your eligible patients.

Screening Mammograms

Who is covered?

Women, age 65 and older or disabled women age 35 and older. All women who receive or are eligible for benefits under Part B of the Medicare program.

How often can screening mammograms be paid for?

The number of mammograms covered is based on the woman's age and her risk status:

Age 35-39: one baseline exam in this period
Age 40-49: one every two years; for high risk women, one every year
Age 50-64: one every year
Age 65 and older: one every two years

What is covered?

Medicare will pay for 80% of the charge for the service that includes the screening mammogram and the physician's interpretation of the results. The limit for the procedure is set at $55. If the services are furnished by a non-participating physician or provider, a special limit applies to the charges made to the beneficiary. In 1991, this limit is 125%; in 1992, 120%, and in 1993, 115%. All coverage is subject to the patient's annual deductible. No physician referral is required.

Cervical Screening

Who is covered?

Women age 65 and older or disabled women age 35 and older. All women who receive or are eligible for benefits under Part B of the Medicare program.

How often can Pap tests be paid for?

Medicare will pay for one Pap test every three years. Women who are at high risk for cervical cancer will be covered for more frequent screenings.

What is covered?

Medicare will pay 80% of the screening Pap test and the physician's interpretation of the test results.

This fact sheet has been prepared by The American Cancer Society, Connecticut Division, Inc., The Connecticut State Medical Society and the Yale Comprehensive Cancer Center (8/91).

Wednesday, November 20, 1991

Ninth Annual Ella T. Grasso Memorial Conference

The Park Plaza, 155 Temple Street, New Haven

This symposium addresses clinical management, therapy, and new advances in gynecologic oncology, and is directed toward obstetricians/gynecologists, medical oncologists, radiation therapists, pathologists, nurses, and residents.

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***Physicians wishing to locate* in Connecticut may call the office requesting opportunities in their specialty. Also, candidates are invited to submit a resume to be kept on file with the Society. An announcement of a physician's availability will be published in two issues of *Connecticut Medicine* as space permits.**

Listing of physicians in the Placement Service does not in any way represent certification by the Society. Investigation of credentials and experience is the responsibility of those seeking applicants for positions.

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The Emergence of Methicillin Resistant *Staphylococcus aureus* in Extended Care Facilities in Northern Connecticut Between 1986 and 1990

ELLIOT L. RANK, PH.D.

ABSTRACT—Methicillin resistant *Staphylococcus aureus (*MRSA) is recognized as a pathogen of significant morbidity in hospital facilities. The microorganism can also be recovered from clinical specimens taken from patients who are residents of extended care facilities (ECFs). This report is a five-year retrospective review of the emergence and spread of MRSA isolates within ECFs located in north central Connecticut and their susceptibility profile over that time span.

Introduction

METHICILLIN resistant *Staphylococcus aureus* (MRSA) is a pathogen of significant morbidity in hospital settings[1,2] and is capable of causing disease similar to methicillin sensitive *Staphylococcus aureus* (MSSA). Residents of extended care facilities (ECFs) or alternative care settings are subject to infections and are treated with antimicrobial therapy in these settings. However, there is an absence of data concerning the prevalence of MRSA and the susceptibility profile of these microorganisms in these settings.[3,4]

The Mount Sinai clinical microbiology laboratory has provided clinical microbiological services to an expanding number of extended care facilities in the north central Connecticut region for many years. A retrospective analysis of the prevalence of MRSA in these institutions was recently completed and presented as part of a seminar program dealing with this microorganism in these facilities.* The data show a significant trend toward increasing prevalance of MRSA and increasing resistance patterns to a number of antimicrobial drugs.

Methods for determining MRSA

All clinical specimens submitted to the laboratory were inoculated onto standardized agar media for growth, enumeration, and identification. *Staphylococcus aureus* isolates were identified as characteristic gram-positive cocci in clusters, growth on Trypticase soy agar with 5% sheep red blood cells, chocolate agar II, Columbia agar with colistin and Nalidixic acid, mannitol salt agar, and no growth on MacConkey agar medium. Individual isolates were tested for agglutination in the Staphaurex reagent (Wellcome Diagnostics, Dartford, England, DA1 5AH), ability to form micro-aggregates of *S. aureus* in the slide coagulase test or clot formation in the tube coagulase test.[5]

The antimicrobial susceptibilities were determined utilizing a well-established and highly standardized automated instrument (Vitek, St. Louis, MO). Methicillin resistance was determined as follows: *S. aureus* isolates were inoculated into Vitek GPS-SA panels to determine minimal inhibitory concentrations to a variety of antimicrobials. The isolate was inoculated onto Mueller-Hinton agar with 4% sodium chloride and 6 mcg per ml of oxacillin (Remel, Lenexa, KA). Isolates capable of growing in the presence of the oxacillin in the Vitek panel or on the agar plate containing oxacillin were referred to as MRSA. Technically, the isolates were oxacillin resistant *S. aureus.* Oxacillin resistance implies methicillin resistance although the reverse is not always true. Data analysis defined an MRSA as one recoverable isolate per patient site per 30-day culture period.

Results

Table 1 shows that two of the 12 ECFs surveyed in 1986 had MRSA isolates (16.7%) with progression to 13 of 19 ECFs surveyed in 1990 (68.4%). Total numbers of MRSA per total *S. aureus* isolated increased from five of 177 (2.8%) in 1986 to 98 of 551 (17.8%) in 1990. The 98 MRSA isolates were recovered from 58 patients (1.7 MRSA recovered per infected patient). This suggested

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*Methicillin resistant *Staphylococcus aureus* in the extended care facility, 17 April 1991, Farmington Marriott, Farmington.

Table 1

Five-Year Survey of MRSA Isolates

Year	*Total ECFs Surveyed*	*Total ECFs With MRSA*	*Total SA*	*Total MRSA*	*Total Patients*
1986	12	2	177	5	4
1987	12	7	240	13	9
1988	16	6	286	17	13
1989	19	8	409	51	27
1990	19	13	551	98	58

SA = *S. aureus*

that either MRSA was recoverable from multiple patient body sites within the 30-day interval, or that successive isolations of MRSA were obtained from individual patients in separate 30-day counting periods.

Table 2 shows the various body sites from which MRSA was recovered. Specimens of urine and decubitus ulcers are the most frequently submitted specimens for culture from residents at ECFs. Decubiti exhibited a steady increase in MRSA from 1986 through 1990 (from 3% to 10.0%). Urine specimens also showed increases in MRSA, but the increase occurred in stages from the 3%-5% range seen in 1987-88 to the 15%-16% range of 1989-90. Sputum cultures showed more than twice the percentage of the urine cultures in 1990 (35.7%). Nares cultures, used to establish the presence or absence of MRSA on residents of ECFs, showed a prevalence of 42.9%-49.3%. This indicates that residents of the affected ECFs can become colonized with MRSA and serve as reservoirs for transmission of the microorganism. Other sites from which MRSA was recovered included the eye, ear, and vagina.

Table 3 shows the overall susceptibility profile for *S. aureus* isolated from ECFs between 1986 and 1990. There was a general trend toward increased resistance for the antimicrobials cephalosporin (first generation cephalosporin class: cephalothin tested), clindamycin, erythromycin, oxacillin, penicillin, tetracycline, trimethoprim-sulfamethoxazole, and ciprofloxacin. Four antimicrobials showed no changes in susceptibility patterns: ampicillin, penicillin, chloramphenicol, and vancomycin. The most dramatic change in resistance was exhibited by ciprofloxacin over the 2.5-year period beginning in 1988 during which more than 50% resistance emerged.

Discussion

Methicillin resistant *S. aureus* is a recognized pathogen capable of causing morbidity and mortality. A recent report suggested that carriers of MRSA were more likely to progress to an infection with MRSA than a carrier of methicillin sensitive organisms or a noncarrier.[3] In the past, the majority of antimicrobial resistance trends emerged from analysis of hospital data. However, a significant proportion of hospital patients are released to ECFs while receiving antimicrobials, other individuals will choose to become long-term residents of ECFs, and virtually all residents of ECFs receive antimicrobials at some point during their stay. Yet antimicrobial resistance trends are not well documented in ECFs.

MRSA is present in ECFs located in northern Connecticut. Their spread has been considerable within and between ECFs in the last five years. Our analysis showed MRSA is recovered from external body orifices, body lesions, and body fluids, such as urine and sputum, indicating the potential for systemic infection in patients.

The most efficient mode of transmission of MRSA between individuals is direct contact. Barrier precautions are useful in preventing direct contact transmission of MRSA between the patient and the care giver. Isolation and treatment of a patient infected with MRSA is useful when there are relatively few cases in an ECF to make patient quarantine manageable. However, isolation becomes impractical when the institutional prevalence of MRSA extends beyond a few manageable cases. In this study and others[3] colonization rates up to 50% of *S. aureus* isolates were MRSA. In the ECFs where this is true, only heroic eradication programs, including extensive education and treatment, would protect residents from future infection and staff members from continuing the chain of transmission.

MRSA is problematic because of its inherent bacterial virulence and the emergence of resistance to microbial agents other than methicillin. A surprising observation was the rapid drop in ciprofloxacin susceptibility to under 50% for *S. aureus*. This may be an unexpected result of greater physician reliance and prescribing of fluoroquinolones for gram-negative infections. Caution is urged in the use of these antimicrobials.[6]

The demographic data and antimicrobial susceptibility profiles described in this study were stored as archival records from highly standardized antimicrobial suscepti-

Table 2

MRSA Per Total *S. aureus* by Site

Specimen Site	*1986*	*1987*	*1988*	*1989*	*1990*
Decubiti	3/91 [3.3]	9/128 [7]	8/129 [6.2]	11/141 [7.8]	22/206 [10.7]
Urine	0/24	2/42 [4.8]	2/64 [3.1]	22/143 [15.4]	30/181 [16.6]
Sputum	2/20 [10]	0/28	4/31 [12.9]	4/37 [10.8]	10/28 [35.7]
Nares			1/3	12/28 [42.9]	35/71 [49.3]
Eye	0/26	0/29	0/40	1/46	0/47
Blood	0/2	0/1	0/3	0/5	0/2
Ear	0/2	0/3	1/4	0/3	0/1
Throat	0/5	0/2	0/2	0/2	0/2
Stool	0/5	0/3	0/5	0/3	1/3
Urethra	0/2	0/2	0/0	0/2	0/4
Vaginal		2/2	1/4	1/3	0/6
Synovial fluid			0/1		
Totals	5/177 [2.8]	13/240 [5.4]	17/286 [5.9]	51/413 [12.3]	98/551 [17.8]

*Figures within square brackets are percent MRSA per total *S. aureus* isolated.

bility testing. Retrospective analyses of data usually attempt to answer questions that are posed after the collection of data. Thus, bias can be encountered in the way the question is posed; a better approach is a prospective study, posing the question first and then collecting the data. However, the purpose of an archival review of antimicrobial susceptibility testing is to spot trends in resistance patterns; there is no doubt that this study showed increasing resistance among various antimicrobial classes over a five-year span when tested against *S. aureus*. The clinical implications for residents of ECFs are very clear: a resident may be exposed, colonized, and possibly infected with MRSA; and MRSA may infect multiple body sites or linger chronically in a single infected site; and, increased resistance to a variety of antimicrobials capable of eradicating the MRSA limits the available treatment choices. A prospective study is warranted to determine whether the increase in MRSA and resistance patterns in ECFs can be reversed. Aggressive changes in ECFs may be necessary, including; immediate cultures of patient specimens when infection is suspected and the prompt replacement of ineffective or resistance-inducing antimicrobials with effective but nonresistance-inducing drugs. Finally, MRSA has been shown to reside in hospital settings for years. ECFs will need the active participation of a working team of hospital-based consultant specialists in pharmacy, infectious disease, microbiology, and infection control to utilize their collective experience and knowledge in reversing the ominous trends associated with MRSA.

Table 3

Five-Year Antimicrobial Resistance Survey in ECFs

	AMPICILLIN	CEPHALOSPORIN	CHLORAMPHENICOL	CLINDAMYCIN	ERYTHROMYCIN	OXACILLIN	PENICILLIN	TETRACYCLINE	TMPSMX	VANCOMYCIN	CIPROFLOXACIN
1986	14.1	96.6	100	97.2	89.3	97.2	13.5	94.9	N.T.	100	N.T.
1987	14.2	91.6	99.5	95	87.9	94.6	14.2	92.9	N.T.	100	N.T.
1988	14.3	91.3	99.6	92.3	80.1	94.1	14.3	87.1	100	100	100
1989	16.6	83.6	99.5	97.3	68.7	87.5	16.1	81.4	94.8	100	79.2
1990	N.T.	75.2	100	92.3	68.1	82.2	10.9	79	87.1	100	48.5

TMPSMX =trimethoprim-sulfamethoxazole
N.T. = not tested
Note: TMPSMX and Ciprofloxacin testing began midyear in 1988.

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Abstracts: First Annual Research Program

NEWINGTON CHILDREN'S HOSPITAL

Introduction

Completed research and works-in-progress were presented at an afternoon program on Research Day, 28 November 1990, which featured 11 oral presentations given by staff members of Newington Children's Hospital, investigators of approved projects, and the Pediatrics Department at Hartford Hospital, and during Research Week, 26-30 November, which featured five poster exhibits. (Abstracts from all of the oral presentations and three of the poster displays are printed here.)

The Golden Question theme was introduced during Research Week and will be carried out each year in a series of special awards called the "Order of the Golden Question for Excellence in Research." Golden Question plaques for the First Annual Research Program were awarded to :

- **Elizabeth Muik for the oral/slide presentation, "The Quantification of Orthotic Perfomance."**
- **Laura Inselman for the poster presentation "Effect of Obesity on Lung Function in Children."**

In addition, Honorable Mention certificates were awarded to:

- **Bonnie Schneider for the oral/slide presentation, "Effect of Dialect on the Determination of Speech Reception Thresholds in Spanish-Speaking Children."**
- **Gregory Javornisky for the poster presentation, "Personality Characteristics in Children with Seizure Disorders."**

Marianna Nelson, Program Committee Chairperson and Research Coordinator at Newington Children's Hospital, wishes to thank committee members Emily O'Neill and M.B. Ozonoff, and Zane Saunders, Institutional Review Board Chairman; Julius Landwirth, Vice-President for Medical Affairs, and John W. Leavitt, Chairman, Board of Directors, NCH Corporation, for their creative ideas and helpful assistance with this program.

Separation of Growth Plate Chondrocytes by Density Gradient Centrifugation: A Novel System for the Study of the Regulation of Bone Growth and Calcification

DENNIS E. CAREY, M.D.

In order to study the effect of hormones and growth factors on bone growth and endochondral ossification, a system has been developed using density gradient centrifugation to separate growth plate chondrocytes into subpopulations at different stages of maturation. Bovine fetal growth plate cartilage was collagenase-digested and the isolated chondrocytes separated into six distinct bands, pre-A (least dense), A, B, C, D, E, (most dense). Subpopulations (B-E) have been plated in subconfluent, high density, and micromass cultures and the following cellular and matrix components analyzed under serum-containing and serum-free conditions after two to three weeks: DNA, alkaline phosphatase activity, type II collagen C-propeptide, hyaluronic acid, thymidine incorporation, sulfate incorporation, and calcium incorporation. In serum, subpopulations in micromass and subconfluent cultures initially show evidence of differentiated chondrocyte function, but after the first week markedly proliferate and dedifferentiate. High density cultures demonstrate decreasing proliferation and increasing alkaline phosphatase activity with decreasing serum concentration. These effects are most prominent in the B band (largest, most mature) cells and are maintained for at least two weeks. The B band cells exhibit evidence of mineralization at day 12 but only in the presence of serum. In conclusion, distinct subpopulations of precalcification growth plate chondrocytes which maintain their chondrocyte phenotype in serum-free culture have been obtained. The system should permit the investigation of the regulation of chondrocyte maturation (ie, hypertrophy) and mineralization. Such studies are critical to the understanding of bone growth and calcification and may eventually lead to treatment of skeletal dysplasias and novel methods for promoting fracture healing which also occurs by endochondral ossification.

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Effect of Dialect on the Determination of Speech Reception Thresholds in Spanish-Speaking Children

BONNIE S. SCHNEIDER, M.S.

Lack of availability of standardized test materials for audiological assessment of Hispanic children poses a significant problem for clinicians. Along with pure-tone screening, speech reception threshold (SRT) testing is a basic method for making such assessments. I examined the possibility that the dialect utilized in presenting Spanish words as stimuli for SRT testing might influence audiological outcome. The present study develops an instrument for determining SRT in Spanish-speaking children, tests its dependence on dialect, and validates it against pure-tone audiometry.

Spanish word lists spoken in Castilian, Caribbean, and Mexican dialects and pure tone averages were compared as stimuli for the determination of speech reception thresholds (SRT) in 12 six-to-seven-year-old Spanish speaking, Puerto Rican children using a balanced crossover design. No statistically or clinically significant differences in threshold were found among dialects. All produced SRTs that were two decibels lower ($p<0.01$) than pure tone but highly correlated with it (Spearman rank correlation coefficient >0.85).

The results indicate that dialect is of minor importance in SRT testing of Puerto Rican children in this age group and suggest that it is not necessary for those performing SRT testing in such children to be proficient in Spanish.

Audiology Supervisor, Department of Speech Pathology and Audiology, Newington Children's Hospital.

Children's Perceptions of Therapeutic Holding on an Inpatient Psychiatric Unit

PATRICIA CABLES, R.N., M.S.N.

This qualitative study explored and identified psychiatric inpatient children's perceptions of therapeutic holding, a human restraint in which staff physically hold a child to contain out-of-control behavior. Ten nonpsychotic school-age children hospitalized on a child psychiatric unit were interviewed using a semistructured instrument created by the researcher. The instrument was pretested on a sample of four nonhospitalized school-age children and presented in a booklet format as a projective means of facilitating participants' self-expression. Content and development appropriateness of the tool was validated by two psychiatric clinical nurse specialists and a clinical psychologist with nationally recognized expertise in providing external controls for ego-impaired children.

Children were invited to participate within 24 to 72 hours following their experience of holding within the milieu. Demographic data were collected and global patterns were assessed. Children's responses were analyzed by the constant comparative method. The themes that merged from the interviews were compared to the concepts of Winnicott's holding environment.[1] Categories that demonstrated interdependence between child and caregiver were anxiety, ambivalence, precipitating anger, fear, need for external control, safety, and mutuality. Categories that were potential impediments to the child's sense of a holding environment included sense of assault, pain, re-creation of sexual issues, sadness, helplessness/hopelessness, and anger with the staff. This pilot study suggests the importance of assessing each child's unique experience of therapeutic holding to enable nursing staff to provide an environment that facilitates development.

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Evaluating the Validity of the *Oxylog* in Adults and Children at Rest and Self-Paced Walking

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The method of choice for measuring oxygen consumption (VO^2) varies according to type and location of activity tested, sample size, and availability of funds. The Oxylog (P.K. Morgan Instruments, Inc.) is a portable instrument that measures VO^2 (liters/min) and inhalatory ventilation (V^i liters/min). The objective of this study is to evaluate the measurement capabilities (ie, VO^2 and V^i) of the Oxylog by comparing data collected in this laboratory to previously reported work.

To date, 12 able-bodied adults and five children have participated in this study. The VO^2, V^i, and heart rate (HR) were recorded every minute for five minutes while the subjects sat quietly. The subject then walked at a self-selected pace along a level circular pathway (30-foot diameter) for five minutes while these same parameters were recorded.

A cursory comparison of these preliminary data with previously published work[1,2,3] is encouraging with an average percentage difference between compared parameters of approximately 15%. These differences may diminish when the sample size is increased and methodology variation is accounted for. These preliminary results suggest that the Oxylog and the present protocol tested are clinically valid and may be used for assessing energy cost in different patient populations.

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	Age *(yr)*	*Height* *(cm)*	*Weight* *(kg)*	*Resting* *VO^2* *(ml/kg/min)*	*Walking* *VO^2* *(ml/kg/min)*	*Energy Cost* *(ml/kg/m)*	*Resting HR* *(bpm)*	*Walking HR* *(bpm)*
Adults	**(n=12)**							
mean	32	174.0	71.0	3.1	9.0	.12	68	88
S.D.	9	10.2	12.6	.6	2.3	.02	13	13
Children	**(n=5)**							
mean	9.8	141	37.5	5.1	12.1	.20	85	102
S.D.	1.3	6.8	4.4	.88	1.2	.03	9	7

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The Determination of Joint Moments: Methodology Verification

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The determination of joint moments of force is a relatively straightforward process with a well established theoretical basis in Newtonian mechanics when given appropriate kinematic and kinetic data as input.[1,2,3] Consequently, the validity of any estimate of the instantaneous joint moment is based on the strength of the algorithm(s) used to estimate the joint center locations, and the accuracy in determining the point of application of any externally applied forces or moments, the anthropometric relationships associated with segmental mass, mass moment of inertia, and center of gravity location. This paper describes the clinical verification of a system to determine the three dimensional joint moments at each lower extremity joint during the gait cycle. An instrumented lower extremity prosthesis provided a direct measure of the reaction joint forces and moments at the knee and ankle, while a computer-controlled optical motion measurement system collected kinematic and kinetic data required to compute the corresponding theoretical joint reactions. In this way, the validity of both the motion measurement system and the data reduction algorithms associated with the determination of the joint moments were evaluated.

The kinematic (eg, 3D joint center locations) and ground reaction forces for the calculation of the joint moments were obtained with the motion measurement system located in the Gait Analysis Laboratory. The measurement system employs three solid state charge coupled device cameras which collect pulsed infrared reflections from passive markers placed on the subject (an 83 kg male above-knee amputee). Ground reaction forces were collected using two force platforms (Advanced Mechanical Technology, Incorporated, AMTI). The six channels of transducer output (described below) were collected simultaneously at a rate of two kilohertz.

A multicomponent force/moment dynamometer (Model SRMC 3A-6-500, AMTI) was mounted on the shank pylon of the above-knee prosthesis to measure directly the joint reactions at either the knee or the ankle. The transducer was mounted proximally or distally on the shank such that the active face of the transducer was closest to the joint of interest. This facilitated the transfer of the measured force and moment components from the measurement site to the joint. That is, since the mass (and inertia) of the coupling between the transducer and joint was small (<5% of the shank/foot assembly), simple equilibrium relationships were used to transfer the measured loads to the joint centers. The mass, mass moments of inertia, and locations of the center of mass of the prosthetic shank and foot were measured and made available for the theoretical calculation of the joint reactions.

The results demonstrate the capability to provide sufficiently sound data for the clinical determination of the joint moments based on Newtonian mechanics. As might be anticipated, the computational technique demonstrated the best reliability in the sagittal plane of the joint (with a mean percentage difference of less then 4%) and more variability in the coronal and transverse planes of the joint (with mean differences of approximately 6% and 7%, respectively). Ongoing examination of the joint moment algorithm includes a consideration of the sensitivity of the method to perturbations in joint center locations, mass/inertia estimates, and velocities and accelerations.

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The Quantification of Orthotic Performance

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The lack of objective information in evaluating the performance of an ankle-foot orthosis has led to research in orthotic performance quantification by the Rehabilitation Engineering Department. Our first objective was to design a device that would allow an orthotist to: (a) measure the ankle angle of an orthosis dynamically (ie, while a patient walks) without the use of long cables or invasive hardware, b) set a reference ankle angle of clinical interest to the orthotist, and c) provide auditory feedback each time the measured ankle angle was greater than (or less than) the reference. These objectives have been achieved in the first generation of the orthotic performance evaluator (OPE).

To improve the clinical usefulness of OPE, a second generation has been designed and is currently being fabricated for clinical evaluation. This version includes the following added features: a) a more flexible sensor technology to measure ankle angle, b) memory of the total dynamic range of motion at the ankle, and c) memory of the minimum and maximum ankle dorisflexion-plantarflexion angle achieved during gait. The ability to record and display these data numerically will provide an orthotist with not only auditory feedback indicating motion beyond (or below) the desired limits but it will also quantify the amount of excess motion (or lack thereof).

Since OPE was developed in conjunction with orthotists in the Orthotics and Prosthetics Department and according to their clinical protocols, these measurement devices will provide more useful information than generic electrogoniometers from which an orthotist can deliver an orthosis with greater confidence or make modifications to his/her design with more direction.

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The Effects of the Rectus Femoris Transfer on Gait in Children with Cerebral Palsy

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The rectus femoris (RF) transfer and release are procedures commonly performed on children with cerebral palsy to improve knee sagittal plane motion. The improvement of knee sagittal plane motion as a result of the transfer has been well documented. It is unclear, however, which particular type of transfer is most effective and whether the release, which is an easier procedure to perform, shows similar results to the transfer. Therefore, the purpose of this study was to evaluate a relatively large group of RF transfer and release patients to determine the following: 1) the effect on sagittal plane knee motion, 2) the effect of the transfer as compared to the release on sagittal plane motion, 3) the effect of the transfer on transverse plane motion, and 4) the prerequisites for an "improved" outcome.

Pre- and one-year postoperative gait analysis data including joint kinematics, electromyography, and temporal and stride parameters were collected. The knee range of motion (ROM), maximum flexion, time of maximum flexion, maximum extension, and angle at initial contact were assessed. The transverse plane changes were evaluated using hip rotation and foot progression angles. A total of 110 patients was assessed in the transfer group and 21 patients in the release group. Each group was divided according to preoperative knee ROM (< or > 80% normal). All patients underwent multiple soft tissue and bony surgical procedures at the time of the RF procedure. A control group (n=19) of cerebral palsy patients who underwent similar procedures but did not have a RF procedure was included.

Preliminary results may be summarized as follows:

1) When preoperative knee sagittal plane motion was at least 80% normal, no change in knee motion in either the transfer or release groups was seen postoperatively.
2) When preoperative knee motion was less than 80% normal:
   a) an increase in sagittal plane motion was observed primarily due to an increase in knee extension in stance,
   b) an improvement in time of peak knee flexion in swing was observed.
3) There were no differences in the parameters measured in terms of the type of medial transfer (ie, to gracilis, sartorius, or semitendinosus).
4) The RF release was not as effective in restoring sagittal plane motion when preoperative motion was less than 80% of normal.
5) The RF transfer (when not accompanied by bony surgery) does not produce any consistent transverse plane changes postoperatively.

It appears that the RF transfer should be included with other appropriate surgical procedures in order to improve knee sagittal plane motion when preoperative knee motion is less than 80% of normal. In a similar preoperative patient group the RF release is not as effective in improving sagittal plane motion. The RF transfer is not an effective substitute for bony surgery in improving transverse plane motion. The results of this study should be taken into consideration when planning surgical procedures.

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Manual Versus Quantitative Muscle Testing in Patients with Duchenne Muscular Dystrophy

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Manual muscle testing, along with other tests, is useful to delineate the natural course of Duchenne muscular dystrophy (DMD) from the onset of symptoms to the loss of ambulation, but it is not a sensitive measure during the late stages of the disease. Quantitative muscle testing using a fixed myometric system, because of its ability to measure very small amounts of tension and compression accurately, should be more sensitive for testing strength in very weak patients with DMD or spinal muscular atrophy. This study is meant to compare the sensitivity of the two types of muscle testing.

Thirteen nonambulatory patients with DMD were evaluated by manual muscle testing using the scale developed by the Collaboration for Investigation of Duchenne Dystrophy and by quantitative muscle testing with the fixed myometry system developed by the Dallas/Cincinnati/Newington Spinal Muscular Atrophy Group. Ten muscle groups that the two protocols had in common were tested. A two-way analysis of variance was used to analyze the total scores of the individual patients.

Preliminary data from pilot tests performed in 1989 suggested that the fixed myometry system provided a more sensitive method of measuring strength in the very weak patient. The data from the 13 patients tested in this study, however, show the two methods to be equally able to separate one patient from another, and, therefore, equally sensitive.

Neither manual nor quantitative muscle testing is, at this time, sensitive enough to show changes in the very weak patient. Clinical research projects to assess changes over a short time period should be restricted to stronger patients until better methods are developed.

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Prevention of Transfusion Associated Cytomegalovirus Infection in Neonates by Removal of Leukocytes from Blood

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The principal methods employed to reduce the risk of transfusion acquired cytomegalovirus disease (TACMV) have been to transfuse only blood and cellular blood components that test negative for antibodies to the cytomegalovirus (CMV) or to administer deglycerolized frozen red blood cells (DFRC). The objective of this study was to determine if filtration techniques to remove leukocytes from blood would reduce or eliminate the risk of TACMV in an at-risk study population which consisted of 50 low-birth-weight ($\leq$1,250 gms) neonates born to CMV seronegative mothers.

Twenty-two of the neonates studied received blood which was filtered in the laboratory through a leukocyte-depletion filter, and 28 received blood prepared by a spin-cool-filter technique. The leukocyte depletion methods used have been reported to remove approximately 98% and 95% of the leukocytes from blood respectively. The donor population providing the blood has a CMV antibody prevalence of 40%.

At the time of discharge and/or two to six months later, 49 of the 50 neonates had negative CMV antibody serologies and/or a negative urine culture for CMV. The only neonate who received IV immunoglobulin seroconverted transiently but urine cultures were negative and none of the 50 had clinical evidence of CMV infection.

The use of a leukocyte depletion filter or the spin-cool-filter technique to reduce the number of leukocytes in the blood prepared for transfusion to seronegative low-birth-weight neonates appeared effective in preventing transfusion transmitted CMV.

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Geographical and Temporal Distribution of Babesial Infection in Connecticut

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Human babesiosis was first recognized in Connecticut in 1989, nearly 15 years after Lyme disease, a similarly transmitted spirochetosis, was detected in the state. To determine the seroprevalence for the babesial pathogen and whether it was recently introduced, we used an indirect immunofluorescence assay to test for *Babesia microti* antibody in 1,285 Connecticut residents. Four groups were studied: I, individuals seropositive for Lyme disease, tested from 1986-89; II, randomly selected outpatients tested in 1989; III, college students residing in Connecticut, tested from 1959-1989; and IV, healthy persons without tick exposure or Lyme disease, tested in 1989. *Babesia* seropositivity was significantly higher in Group I (9.5%; n=735) than in Groups II (2.6%; n=304, P <0.0001) and III (1.0%; n=206, P <0.0001) but not Group IV (2.5%; n=40). *Babesia* seropositivity for Group I ranged from 9.2% to 10.2% between 1986 and 1989, and *Babesia* seropositivity for Group III ranged from 0% between 1959 and 1985 to 2.9% between 1986 and 1989. There is a considerable risk of babesial infection among residents of mainland Connecticut who are seropositive for Lyme disease, a risk that appears to have remained constant over the past five years.

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The Effects of a Selective Dorsal Rhizotomy on Gait in Children with Cerebral Palsy

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One of the major problems in the child with cerebral palsy is a resistance to movement that is due to an increase in muscle tone. A selective dorsal rhizotomy is a neurosurgical procedure performed to reduce this high muscle tone. The purpose of this study is to assess quantitatively the effects of a selective dorsal rhizotomy on the child's gait pattern.

Thirteen children (ages four to 10 years) with a diagnosis of cerebral palsy underwent gait analysis before and after a selective dorsal rhizotomy. A clinical examination, gait kinematics, temporal and stride parameters, as well as EMG data, were obtained during each analysis. Paired t-tests were performed to test for differences before and after rhizotomy.

There was a significant reduction in hypertonicity as assessed through ankle clonus and a Duncan Ely test. Notable changes in passive joint range of motion were seen (see table). During gait, the majority of changes were seen in the sagittal plane, with an increase in knee flexion in swing, ankle dorisflexion in stance, and anterior pelvic

tilt. In the transverse plane, an improvement in foot progression was seen. With respect to gait, this means that the child may have better swing phase clearance and a more plantigrade foot. These are two critical prerequisites of normal gait.

In the future we hope to be able to select specific gait parameters which will enable a better prediction of the postoperative ambulatory status of the child undergoing rhizotomy.

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Passive Joint Range of Motion

Range of Motion	*Normal*	*Preop.*	*Postop.*	*Change*
Distal hamstrings	0°	-52° ± 11°	-37° ± 9°	15° ± 10°
Hip abduction	0°-45°	26° ± 11°	36° ± 8°	10° ± 10°
Hip estension	0°	-14° ± 7°	-9° ± 9°	5° ± 9°
Dorsiflexion	0°-20°	7° ± 9°	12° ± 8°	5° ± 10°

Effect of Obesity on Lung Function in Children

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The effects of obesity and subsequent nutritional intervention on lung function were studied in six children, age 11-15 years, with 189-271% of predicted ideal body weight and 35.1-54.2 kg/m^2 body mass index. Individuals with specific organic etiologies of obesity were excluded. The subjects were examined while sitting and had measurements of lung volumes, airflow rates, single breath diffusing capacity (DLCO), and maximum thoracic muscle strength during inspiration (PImax) starting at residual volume (RV) and during expiration (PEmax) staring at total lung capacity (TLC). When compared with predicted normal values for sex, height, and body surface area, decreases (mean±SE, percentage of predicted) were observed in vital capacity (VC, slow: 81±7; forced: 77±7), forced expiratory volume in one second (FEV1, 66±6; FEV1/FVC, 78±10), forced expiratory flow rate (FEF25-75%, 64±15), maximal voluntary ventilation (MVV, 60±8), expiratory reserve volume (40±10), absolute DLCO (42±6) and DLCO/alveolar volume (67±4). Increases occurred in RV (161±18) and RV/TLC (38±2). Functional residual capacity, TLC, PImax, and PEmax were normal. Only one patient had ≥10% increase in airflow rates with postbronchodilator testing. Following an 8-19 kg weight loss in three children one to three months later, elevations in baseline values were observed in FVC (18%), FEV1 (20%), FEF25-75% (21%), and MVV (36%). Other measurements did not change. Thus, altered lung function occurs in obese children and is characterized by air-trapping with large and small airway narrowing, restrictive lung disease, and a reduced DLCO. The large and small airway narrowing improves with short-term weight-loss, while diminished DLCO does not. The airway and MVV alterations may be secondary to extrinsic mechanical compression causing reduced chest wall compliance and increased work of breathing and/or intrinsic changes with lipid deposition in the lung.[1] Reduction in the DLCO may reflect decreases in alveolar surface area relative to lung volume[2] and may be permanent despite weight loss during early-to mid-adolescence.

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Effects of a Physical Handicap on Effectance Motivation

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Children derive pleasure from activities requiring mastery of the environment and achieve the greatest satisfaction when optimally challenged. This phenomenon has been called effectance motivation and although it has been studied with respect to verbally challenging activities, few studies have investigated it with respect to motor activities. Moreover, very little research has been conducted on effectance motivation in a physically impaired population. The purpose of the present study has been to investigate the effect of a physical handicap on effectance motivation with respect to verbal and motor activities. It was hypothesized that: a) mildly handicapped children will demonstrate a higher level of effectance motivation on motor activities than their more severely handicapped peers, and b) degree of physical handicap will not affect level of effectance motivation with respect to verbal activities. Forty children between the ages of six and 13 years diagnosed with cerebral palsy will be included in the study. Children are administered a basketball and a riddle task of increasing difficulties. After each task, children are asked to rate their level of enjoyment at three levels of difficulty: a) the easiest level, b) the most difficult level at which they were successful, and c) the level at which they were no longer successful. Effectance motivation is evidenced when a child reports greatest enjoyment at the most difficult level at which they are successful. Thirty-seven children have participated in the study to date and preliminary inspection of the data reveals support for both hypotheses. It is expected that more formal statistical analyses to be conducted upon completion of data collection will contribute to a more comprehensive understanding of effectance motivation.

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Personality Characteristics in Children with Seizure Disorders

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Personality profiles of children with seizure disorders were compared to children with seizure-free neurologic disorders. Findings of the Personality Inventory For Children - Revised (PIC-R) indicate that seizure disordered children have significantly greater discipline, self-control, and delinquency problems. For those with EEG-based temporal lobe focus versus those with a seizure focus elsewhere, significantly higher scores were obtained on the hyperactivity scale (mean 13.5 and 11.0, respectively; t=2.28, p=.03). This was also true for overall psychological adjustment scales (mean=28.6 versus 20.5, respectively; t=2.17, p=.04). In contrast, significant alteration in cognitive and intellectual underpinnings of personality and high levels of anxiety were associated with a frontal lobe focus when compared to seizure focus elsewhere. Mean scores for Intellectual Screening for children with frontal lobe focus was 19.2 versus 15.1 for patients without a frontal lobe seizure focus (t=2.10, p=.05). Mean scores for Anxiety Scale were 11.1 for children with frontal lobe focus versus 6.5 for children without (t=2.06, p=.05). The PIC-R has clinical utility in identifying personality problems of seizure-disordered children, including those associated with anatomically different foci.

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On Bad Doctors

MICHAEL A. LACOMBE, M.D.

THE narrow road from Épinal to Provènchères is the most direct route and the most enchanting as well. Leaving the calm predictability of the upper Moselle, its asphalt races eastward seemingly without purpose, hardly noticing the licks and swirls of the Mortagne or the heavy warning of the chapel bells at Bruyères. Only after St. Dié does the road, now shaded on either side by the forest of the Vosges, slow to the climb ahead. Leaning first to this curve and now back into a leftward ascent, as though undecided about the sanctuary of the mountains, the road at last opens to the summit ridge and its clear views both east and west.

It was to this place of contemplation that Jean-Paul and Michel had traveled one rainy Monday night. There was a restaurant, of course. One never heads directly into the light, but rather assumes a more tangential course, with insight dealing a glancing blow. The only restaurant at Provènchères, called simply *Vosgienne*, was a treasure. From the outside it crouched hut-like, built low as it was against the wind. The light from its small-paned windows drew its guests within as does a church its faithful.

"How does he do it?" asked Michel. "This *potage Parmentier* is sheer perfection. Marie-Phillippe amazes me every time. A few simple potatoes and leeks, and he gives us this!"

"Commitment, Michel, commitment," answered Jean-Paul, slurping his soup. "Marie-Phillippe could dazzle us with his entrées and anyone but you, my friend, might then excuse an ordinary soup course. But it is not for you that Marie-Phillippe cooks his soup. He cooks for his God."

Michel turned to look at the fire in the great stone hearth. The corners of his mouth sagged. He tossed one hand, then the other, looked at his friend across from him, then back into the fire.

"But not everywhere do we find this commitment, eh? Even with the greatest of chefs, there is a danger at the destination....What has happened to Roland, Jean-Paul? What do you make of it? I have known him my whole life, it seems. But he is a stranger to me now."

The west wind rattled the linden branches against the window panes outside. Jean-Paul assumed a tortured look and stalled for time.

"Happened? What do you mean, 'happened?'"

"Marianna and I went to Besançon two weeks ago for dinner. To be sure, his parking lot is more overflowing than ever—he has gone to three sittings—and the *Auberge Doubs* impresses as never before. One sees its lights from miles away. Roland has a red canopy 10 meters long at the entry-way, with red carpet, no less. There is an initial excitement, a specialness one senses on first arriving. But, then...."

"Roland was my best friend, Michel," interrupted Jean-Paul sternly. "He and I were classmates."

"He was at the *école Hôtelière*?" asked Michel.

"Their best pupil in his day. Leagues ahead of the rest of us. Innovative...brilliant...daring."

Jean-Paul interrupted to direct their waiter, "The *matelote* for me, the *foie gras* for Michel. *Merci*."

"Excuse me, my friend, and do not take offense, but you would not know his greatness now. Roland has lost the stamp of Strasbourg. Oh, he is making lots of money, *oui*, and old man Gaertner would be proud of that, I suppose. But I cannot admire him or own to be of the same profession."

Jean-Paul hesitated, then said, "I have not been to Besançon for years....Roland and I had a falling out. Still, he is an old friend. But...what did you see there?"

"I saw a man without caring. I saw patrons run in and out like cattle, given no time, no pause, no consideration.

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I saw a machine for making money, a *terrine de volaille* made of paste and straw and little else, a *feuilleté* tasteless, made only for show. I saw a man trading on the knowledge that *once* he had three stars, that *once* he had trained in Strasbourg, that *once* he had been the most renowned chef in Alsace, in all of eastern France, that *once*..."

" 'Let he who is without sin cast the first stone,'" interrupted Jean-Paul.

"You compare me with Roland!? How can you say that *l'Ange* is like his...his...factory? How can you insult my family like this!?" Michel was standing, pointing a finger, napkin on the floor. The small dining room grew suddenly still. Marie-Phillippe could be seen in the kitchen doorway. He knew these two. Dinner with them was never a dull affair.

"I meant none of those things, *mon ami*. I mean only that all of us, even you, could lose the way as Roland has. We all share that capacity."

Michel sat down, permitting himself to cool. The other diners resumed their meals.

"Lost his way," he said. "Well-put. Roland has lost his way."

Jean-Paul held his soup dish out for the waiter, nodded and smiled slightly to him, and turned back to Michel.

"What is Roland's reality?" he asked his friend. "How does he measure his life? By what parameters?"

Michel pondered the question. He turned to reflect upon his own reality. At an adjacent table sat a young family of four, parents attentive, children wide-eyed, exploring the world Marie-Phillippe had created for them. The little boy, in red bow-tie, knife and fork in either hand, confronted his *cuisse de grenouilles*, planning his attack. His sister, younger still, held the empty shell of an *escargot* aloft, as if to coax forth one last snail. Michel felt the harmony of these four, sensed their health and vitality, knew the happiness they would gain from this togetherness, advanced in some small way by Marie-Phillippe's *ambiance* and gift of perfection. At a corner table, discreetly tucked away, sat the young lovers. Every dining room has them, and every *maître d'*, the responsibility for their correct situation. Michel had watched them started on proper course, guided ever so gently away from the expensive champagne and toward a more palatable—and more affordable—*pétillant* Vouvray. She, with charming douceness, hangs on his every word. He, strong and bold, paints the air with his gestures as he tells her of the world. Then, a pause, their eyes meet—she looks down, smiles demurely. He takes her hand.

And at the table by the fire, Michel watched an elderly couple, bathed in the hearth's amber glow, themselves holding hands, talking gently. Directly and full to the face, they behold each other, permitting Michel—and anyone—to see the love and understanding between them.

Who are these people? wonders Michel. Are they customers with fat wallets to be emptied? Strangers with dull palates to be scorned? Or something more? What do these people mean to Marie-Phillippe? And what is his place in their lives?

Finally, Michel turned back to his friend, who had been quietly observing him, and asked, "What was it you said?"

Jean-Paul smiled and said, "I asked you what you thought Roland's reality might be. From what does he derive his identity? How does he define himself in relation to his world? What is important to him, what is *véritable*?"

Michel shifted in his chair, tossed his hand in the air, pinched the wax on the candle, looked about, frowned, scowled, raised his eyebrows, and shrugged.

"The obvious things I would suppose. Money... success...power. His station in life. That, I suppose, is Roland's reality."

"Yes, those goals most compelling...arresting...intoxicating. You remember Odysseus. He lashes himself to the mast, so compelling is the Siren's song. So tempting to all of us. But the song was not always so compelling. Which of us started school with thoughts of 'I will do this thing to make money. I will learn the intricacies of my art so that I may be famous. I will become a great chef so that I may be loved, so that I may be all-powerful, so that I may be redeemed.' Do any of us as young students even *consider* these things? Of course not! Only later, after the battle, when we think the war safely won, when we sail home on calm seas, do we hear the Siren's song. I will tell you Roland's story."

Jean-Paul turned in his chair, stretched and crossed his legs, swirled and sniffed his gewürztraminer, and sat abruptly once again. An immense sadness overtook him.

"Did you know that Johann Sebastian Bach wrote and performed only for the glory of God? He was like our friend here," said Jean-Paul, nodding his head toward the kitchen and Marie-Phillippe.

"Roland's reality, that of ambition, never occurred to Bach. Never did Bach say to himself, 'I will compose *Toccata and Fugue in D* and become rich and famous.' Bach's reality embraced other, higher ideals. Not so, Roland's.

"Roland began modestly enough after the university, as a *sous-chef* in Marlenheim. But Roland always had one eye toward advancement. That was primary. He must make it to a one-star, then *sous-chef* at a two-star, and so on, until he is owner, with his own stars, and so forth. Always he would think, 'When I make to the next step, I will be happy, and I will have more money and more things and that will make me even happier.' Roland's ambition was like the university professor's, who forgets he exists for his students, and rather is forever planning his next career move, his next promotion.

"And of course, happiness never comes. There is always the next move, and more money to earn...no end to it. Roland imagined a treasure chest to be filled for him by life and by his own ambition...with this treasure, he would find happiness and a sense of accomplishment. He never found them, of course; the chest can never be filled. One must look elsewhere. But Roland cannot. He is trapped in this thinking, caring not at all for his patrons, always surrounding himself with more glitter.

"Friends are brushed aside, excellence forsaken, as he pursues this Siren's song. He cannot get off this path."

Michel coughed, as though to interrupt. He began carefully, not wishing for a scene from Jean-Paul such as he himself had caused moments before. He began, "Each of us, *mon ami*, writes his own story, don't you think? Whatever his past, whatever it is that drives him now, do you not suppose that Roland could change? To change paths now would be difficult for him, I admit, especially with his present path so paved in gold...but not impossible."

"Better to start young," answered Jean-Paul, "at university or even before. Choose a higher goal, an *Idéal*, and let nothing stay your course. Perhaps it will be the thirst for knowledge or some grand creative fire within. You, Michel, have your love of people, your sense of harmony to steer you. Marie-Phillippe, his God. And my *pension*, with its *ambiance*, is an expression of the love between Yvette and myself, I suppose. We are lucky. We are this way almost by accident. Roland is not so lucky."

"Providence, perhaps," said Michel. "But we make choices all the time, and those choices are conscious as a rule. I will bore you I know, but I am reminded of a story from *Le Rouge et le Noir.*"

Jean-Paul laughed loudly and slapped the table. Michel was forever quoting his Stendhal. Michel continued, "The hero, Julien Sorel, has an affair with the beautiful wife of his employer, whose children he tutors. He then gains a position in the seminary at Besançon where he studies for 14 months. But he is compelled to return to her, to recapture what he has had with her.

"She, Mme. de Rênal, has meanwhile returned to her faith in God, begging forgiveness for her past sins. With a ladder, Julien gains entry to her bedroom from the garden. She is shocked, appalled, scandalized! With renewed passion, with his awakened love, Julien attempts an embrace. Mme. de Rênal rebuffs him. He pleads, he professes his undying love for her. Still she refuses.

"Then, my friend, he makes his choice. And it is fully a conscious one. He feigns a bitter remorse. He tells her (with a cold heart) of his unhappiness at the seminary, of his endless dreaming of her. Finally, he plays his last card in this game: He is leaving her forever, he says, going to Paris at once and forever. He will never see her again. He moves to the window, to the ladder, as though to leave. Mme. de Rênal can no longer resist. She throws herself into his arms.

"And here Stendhal says a moving thing, in this chapter he calls 'Ambition.'" (Michel was standing now, pointing his finger upward in instruction. The entire dining room sat in rapt attention.)

"Stendhal writes, 'Coming a bit sooner,'—that is, in response to the earlier genuine emotion from Julien—'Coming a bit sooner, this reversion to tender feelings, the disappearance of Mme. de Rênal's remorse, would have meant divine happiness; this obtained, by art, it was nothing more than a triumph.'"

As Michel began to sit once again, the little girl at the next table clapped chubby hands. With a grand sweep of his arm, Michel bowed deeply in her direction. She smiled at him with dancing eyes.

"What begins as some strange calling, or a mother's wish, or a dream, may end, if we are not careful, in a Faustian bargain," said Jean-Claude. "It is time to go...did you smell the mangoes in this Sauternes?"

The storm had passed. Out in the parking lot of the *Vosgienne*, the two friends paused for a moment of stargazing.

"Tell me their names again."

"Look this way then...the brightest first, there yellowish...*Arcturus*. Hippocrates made much of its influence, believing that illness falling under its sign would prove critical indeed. To its left...see the gentle arc of stars and its brightest at the center...*Alphecca* to the Arabs...but for certain American Indians—the Shawnee—she was the wife of White Hawk, our *Arcturus*. All is harmony, *n'est-ce pas*? Now, my friend, above *Arcturus* and slightly to the right, that beautiful star seemingly alone...Cor Caroli...the Heart of Charlemagne...a French star of course, of unparalleled beauty, *naturellement*.

"Far below *Arcturus* and to the right...the very bright one...*Spica*, it's called. Draw a line between the two and to the right of your line, in that empty space there, well, not empty really...that is *The Realm of the Galaxies*... hundreds of them, thousands perhaps, many of them French, no doubt. *Spica* is in *Virgo*, or Persephone, the daughter of Demeter, which is a wonderful story in itself...."

Thus did the two friends lose themselves in the Universe, leaving the gears of the galaxies to grind as They will.

A Practice Abroad (?)

CHARLES SHEARD, M.D., F.A.C.P., F.R.C.P. (C)

AFTER my wife broke her leg skiing the second time, it seemed fairly obvious that we should explore the Caribbean for our succeeding winter vacation. This we did in March of 1969 by chartering a motor-sailor with Captain Cook and doing the Grenadines from Grenada to St. Vincent's and back, covering all the little islands in between. Every morning at 8 o'clock, on the radio, we could listen to various cruise-parties and their captains talking to each other about such mundane things as how to take care of impetigo, insect bites, and the need for spare parts, or reservations for dinner at McIntyre's in Bequia, etc. This free-for-all was appropriately called "The Children's Hour," and much of it was a request for medical advice. "Does anyone have a doctor on board?" Thus began a medical love affair with the Southern Caribbean. The sweetness of the people and their lack of specialty care, the beauty of the islands and the perfection of the climate, all conspired to woo me into an arrangement with the then prime minister of Grenada, Sir Eric Gairy, to do the dermatology for the island of Grenada. The bargain was three or four visits a year in exchange for a license to practice with the possibility of semiretirement for my older years.

Having a narrow specialty, dermatology, meant that I would be helpful to the local doctors rather then competitive. Almost all of the island's doctors had been educated in London, Edinburgh, or Dublin; F.R.C.S., England and Edinburgh, for the surgeons; M.R.C.P., London, for the internists. This is true of the British Caribbean in general. The average physician is capable, but they do miss the eye, E.N.T., urology, and other specialties.

It was no time before I was getting referrals and seeing almost 100 patients a day. I was there for a week or so every three or four months. I cadged drugs from detail men (eg, Syntex) and often could get ready-to-become-outdated Synalar Cream or Ointment which couldn't be sold in the U.S., and I would ship these down by boat before I arrived. I would then hand them out in my "clinic" in the General Hospital of St. George's. Steroid creams are prohibitive in price for all but the very rich on the islands, and this often was a Godsend. The F.D.A. has forbidden this practice now, but on the whole the drug companies were very generous with samples, etc., and I could handle almost all my low-income patients with my own supplies. Sometimes I would ship down large 5 lb. jars of hydrophylic ointment just for the facility of having this in the pharmacies for compounding.

An organization called M.A.P. International, a missionary-oriented charitable organization run by the Baptist Church in Brunswick, Georgia, will supply medication and other necessities such as instruments, gowns, etc., on request. You have to purchase them, but the cost is so low it is practically a give-away. I found, on occasion, that they were very helpful, for instance, in obtaining Selsun for treating tinea versicolor, at a reasonable price, to be given away, of course.

When I began the clinic in 1971, I went down alone, but later took my wife as chauffeur, cook, and delivery gal. The hospital supplied a nurse and clerk to list the patients in a book, and opposite their names I would write the diagnosis and treatment to refer to on later visits. The practice thrived. I equipped my office with an electric typewriter (which I can use rapidly, fortunately) and all referred patients would receive letters for their doctors outlining the proposed scheme of care with alternatives, along with the probable diagnosis. I installed an air conditioner, brought down a microscope, special lamps, electrocautery along with transformers, etc., and loads of intralesional Kenalog. The load of keloids was unexpectedly heavy. One man who had been stung by a Portuguese man-o-war had keloids all around his trunk and arms. I have never seen anything like it before, or since. It took about four years to flatten them down, but we did.

Being a British island, Grenada permitted no fee for medical services, but the minister of health, in view of my expenses in traveling, allowed me to request contribu-

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tions. A small sign states, “A contribution of $3 would be appreciated.” That is about $1 U.S. About half put something in the box, some put in a $20 bill, others 50c, but they were all grateful with an old-fashioned charm and grace that is all too missed at home.

I believe I make a contribution to their health and happiness. Ordinarily, specialty care can be obtained in Barbados or Trinidad, about an hour's flight away; or Venezuela, for leprosy patients, of whom we have about 25 on the island. I remember one man with lepromatous leprosy and a blind wife. He was Dapsone-resistant on 600 mg daily and refused to go to Venezuela. We got him some Lamprene from Switzerland (this was then experimental in the U.S.) and he cleared dramatically. He was very grateful. Another few cases of dermatitis herpetiformis were picked up and are now completely controlled. The satisfaction of knowing you are helpful is immensely rewarding, and not the least of it, is the knowledge by Grenadians that there are American doctors who care about their plight and mean to help. A New York eye specialist, Frank Constantine, has been doing the same thing for years. In fact, the eye specialists have an organization (The Lighthouse) that does this all over the world, I believe. The friendliness resulting from all this is valuable to our government, I am sure, but the main thing is the personal satisfaction you get for yourself.

All of my expenses are tax-deductible: food, rent, car rental, transportation, etc. are all paid for out of my office at home, and the I.R.S. has never questioned any of it. I would strongly recommend this as a cure for the “Practice Blahs” that afflicts so many of us in the mid 50s. If you have a narrow specialty and can fit in with a bunch of local MDs who would like to have your help and guidance, try a tropical island. There are still lots of them. I can assure you you will always feel safe wherever you go. They get to know you much faster than you think, and you will enjoy it. I think it helps to show them that Yankee doctors are not only good doctors, but good people too.

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Leuprolide with Flutamide for Complete Androgen Ablation: Therapeutic Alternative for Advanced Prostatic Cancer (Stage D_2)

ELIZABETH CHIME-UDEH, PHARM. D.

Introduction

THE primary treatments of choice for advanced prostatic cancer (ie, surgical castration/estrogen therapy) have distinct disadvantages that present problems in the management of this disease. The psychological effect of surgical castration can be so severe that men suffering from prostatic cancer have refused such therapy.[1,2] On the other hand, estrogen therapy has severe adverse effects which make it an undesirable alternative.[1] Because of problems associated with these two therapeutic options, new treatment modalities for metastatic cancer of the prostate have been developed.[1,2] These therapeutic advances include: 1) use of luteinizing hormone releasing hormone agonist (LH-RH-A); 2) use of antiandrogens; 3) adjunctive therapy with antiandrogens and cytotoxic agents, and 4) use of combined LH-RH-A and antiandrogenic compounds. Of all the therapeutic options evaluated to date, the combination of LH-RH-A with nonsteroidal antiandrogenic agents holds the most promise as an alternative for the management of stage D_2 prostatic cancers.[1,2] This review focuses on the recently approved LH-RH-A leuprolide (Leupron®) plus flutamide (Eulexin®)[1] in the management of advanced prostatic cancer (stage D_2).

Clinical Pharmacology

Leuprolide, pharmacologically stimulates the release of luteinizing hormone (LH) from the pituitary. LH in turn activates cyclic adenosine monophosphate-proteinkinase resulting in the production of testosterone.[1,3] However, at higher doses or during prolonged administration, LH-RH-As were discovered to antagonize the production of testosterone and impair the function of male secondary sex organs.[1] This is achieved through down-regulation of receptors in the pituitary and the testes.[1,4] The dose dependent paradoxical effects of LH-RH-A formed the basis for their use in the management of prostatic cancer.[1]

Flutamide, a nonsteroidal antiandrogenic agent, produces its pharmacological effect by inhibiting nuclear binding of androgens in target tissues and by depressing tissue uptake and retention of testosterone.[5-7] Because of the combined pharmacodynamic effects of leuprolide and flutamide, they represent an excellent choice for total androgen ablation.

Rationale for Combining Leuprolide and Flutamide

Leuprolide at doses high enough to achieve chemical castration produces a transient increase in serum testosterone. This elevation of testosterone causes tumor flare-up, characterized by severe bone pain and even progression of disease.[8] Also, leuprolide produces its effect primarily through the pituitary gland and does not affect the release of adrenal androgenic compounds.[8] These extrasplanchnic androgens are converted to testosterone in the prostate gland and target tissues.[8] They account for up to 30% of androgenic activity within the prostate after chemical castration with LH-RH-A or orchiectomy.[9] Since total androgen ablation is not possible with these other sources of androgens, antiandrogens like flutamide which act peripherally become promising agents to use in combination with LH-RH-A.

The combination of nonsteroidal antiandrogens and LH-RH-A has additional advantages including: 1) elimination of the psychological stress associated with orchiectomy, 2) reversibility of therapy, 3) elimination of serious side effects associated with estrogen therapy, and 4) lower doses of each drug due to the different mechanism of androgen ablation.[10]

Clinical Trials

Clinical studies using LH-RH-A and antiandrogens to achieve total androgen ablation in patients with advanced

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metastatic cancer have been reported world wide.[11-14] The various studies employed different LH-RH-As and different antiandrogens in an attempt to achieve total androgen ablation. In one double-blind randomized controlled study involving 603 patients, the combination of leuprolide and flutamide was found to be more effective in stage D_2 prostatic cancer than leuprolide alone.[12] The combination therapy was significantly more effective in survival rates, progression free survival, and improvement in performance status.

Other studies using different LH-RH-As plus flutamide or other antiandrogens have been reported.[9,11,13-17] Although the results of most of these studies are encouraging, they are not as conclusive as the leuprolide-flutamide study described above. Differences in patient type, previous therapy, lack of standard criteria for evaluation, and potency of agents have been cited as possible reasons for these results.[12,13]

Studies comparing surgical castration to total androgen block using different LH-RH-As and antiandrogens showed variable responses. Most of the studies showed a better objective response with combination therapy,[16,18,19] but one study showed a statistically significant difference in response favoring the combination therapy.[20]

Adverse Effects

The most common side effects associated with this combination are hot flashes in 63.6% of the patients, diarrhea in 13.6%, gynecomastia in 13.3%, nausea or vomiting in 11.8%, peripheral edema in 4.9%, and loss of libido. Most of the side effects with this combination were attributed to the central effect of leuprolide.[12]

Patient Selection, Dosage, and Cost

Clinical trials with LH-RH-A and flutamide have demonstrated that maximum therapeutic benefit can be achieved in a subset of patients.[10-12,14] These include: 1) patients with minimum disease, 2) patients with good performance status, 3) patients without other poor prognostic factors (ie, weight loss, anorexia, anemia, chronic heart disease), and 4) previously untreated patients. Also, time of starting therapy is important. Starting therapy early rather than late appears to have therapeutic advantage.[8] The Federal Food and Drug Administration recommends that both leuprolide and flutamide be started simultaneously. The approved regimen is leuprolide 1 mg subcutaneously (SC) daily with flutamide 250 mg orally three times a day.[21] Recently a new dosage form of leuprolide (depot formulation) was also approved. This intramuscular (IM) dosage form is designed to eliminate daily SC injections of leuprolide. Clinical trials with this depot formulation have shown that it is as safe and effective as the daily SC formulation in the treatment of advanced prostatic cancer.[22] The FDA approved dose is 7.5 mg IM monthly.

The monthly acquisition cost for the combination therapy is approximately $525.

Conclusion

In summary, the combination of leuprolide and flutamide for the management of stage D_2 prostatic cancer is more effective than monotherapy with either agent in achieving complete androgen ablation. This combination therapy provides a desirable alternative to surgical castration and estrogen therapy for treatment of advanced prostatic cancer. Selection of appropriate patients and early initiation of therapy are important factors in obtaining maximum response to therapy.

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Important Advances in Clinical Medicine

Pediatrics

The Scientific Board of the California Medical Association presents the following inventory of items of progress in pediatrics. Each item, in the judgement of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, or scholars to stay abreast of these items of progress in pediatrics that have recently achieved a substantial degree of authoritative acceptance, whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Pediatrics of the California Medical Association, and the summaries were prepared under its direction.

Diagnosis, Treatment, and Follow-up of Newborns Addicted to Cocaine

THE diagnosis of cocaine in infants is fraught with problems. There is little warning of the birth of an addicted neonate because many women using cocaine receive little or no prenatal care and therefore do not come to the attention of medical professionals until the time of delivery. Although comprehensive, nonjudgemental history taking may identify chemical use, a considerable number of women deny use even when they know they will be screened. Testing itself may not give accurate results because the criteria for selecting persons to be screened vary and because cocaine can be detected in the urine for only a short time.

Universal screening has been studied in two settings. Women obtaining prenatal care who were screened for alcohol, opiates, cocaine, and cannabinoids had a 14.8% prevalence rate. There were no significant differences in overall drug detection between public and private clinics or between African-American and white women, although the frequency of cocaine detection was higher in public clinics and in African-American women. Of greatest concern was the difference found in the rates of reporting these results to health authorities after delivery. African-American women were ten times more likely than white women to be reported, and poor women were more likely than others to be reported. In another study, all obstetrics patients admitted to an inner-city hospital over a one-year period were screened for opiates, cocaine, and amphetamines. The rate was 20.5%, with cocaine the most frequently found drug (46% of positive screens).

Complications of pregnancy and delivery associated with cocaine use are similar to those associated with smoking and poor prenatal care and nutrition. These may include abruptio placentae, premature delivery, and intrauterine growth retardation. In fact, most infants with exposure to cocaine have also had exposure to cigarettes and other potentially harmful drugs, such as alcohol and marijuana. Often cocaine is used in combination with opiates, and affected infants may show signs of narcotic withdrawal. A close examination for evidence of rare malformations or ischemic damage to the heart, kidneys, intestinal tract, and central nervous system, along with supportive care, is usually sufficient for the majority of infants with cocaine exposure. In addition, the possibility must always be considered that a cocaine-exposed infant has also had exposure to sexually transmitted diseases, including hepatitis B, syphilis, gonorrhea, cytomegalovirus, and human immunodeficiency virus. Controversy exists regarding the increased risk for the sudden infant death syndrome in infants with cocaine exposure, and

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recommendations for home apnea monitoring are not uniform.

The long-term follow-up of these infants is essential. Neurobehavioral changes usually occur within the first several days of life and may persist throughout the first year. These include irritability, sleep disturbances, hypertonia, and feeding difficulties. Close follow-up for developmental and behavioral disturbances is warranted through school entry because problems with language development, motor skills, attention span, organizational strategies, and interpersonal interactions have been described. The outcome for these infants as they reach their teens and adulthood is unknown but should be of concern to the medical profession and society as a whole.

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Flexible Fiberoptic Bronchoscopy in Children

FLEXIBLE fiberoptic laryngoscopy and bronchoscopy have become useful techniques in evaluating respiratory disease in infants or children. Both procedures can be done on an outpatient basis. The first instrument developed for pediatric use was the 3.5-mm tip-diameter instrument. This bronchoscope contains a channel for the instillation of topical anesthetics or saline solution and the aspiration of lower airway specimens. It can be passed through the nose of most infants and is appropriate for most pediatric procedures. A small 2.7-mm instrument is particularly well suited to infant laryngoscopy and bronchoscopy but does not contain a suction channel. Topical anesthesia is provided by instillation into the nares of 1% lidocaine and by administering 1% lidocaine onto the larynx and vocal cords, trachea, and lower airway through the bronchoscope channel. A narcotic such as meperidine or fentanyl and midazolam, provided in carefully titrated doses, may also be used. Skill in airway management and respiratory support is required, and monitoring and an environment conducive to ongoing assessment and intervention are essential.

In the outpatient setting, flexible bronchoscopy is commonly done to evaluate airway anatomy. Laryngomalacia, the common finding in infants with stridor, is easily demonstrated by the dynamic view of the larynx provided by the fiberoptic endoscope. Unilateral or bilateral cord dysfunction, glottic hemangiomas, and laryngeal cysts are easily detected by fiberoptic studies. Tracheomalacia is often associated with laryngomalacia and is well visualized after the bronchoscope is passed into the trachea. Vascular compression of the trachea is also easily recognized, as are other malformations in lower airway anatomy. Persistent wheezing in an older child may be an indication for bronchoscopy, especially if there is evidence of localized disease or a low probability of a history of foreign body aspiration. Rigid bronchoscopy rather than flexible bronchoscopy is, however, indicated for foreign body removal in children. In addition, rigid bronchoscopy is required for the biopsy of endobronchial lesions and is preferred when difficulty in establishing or maintaining the airway is anticipated.

Laryngoscopy and bronchoscopy are equally useful procedures in children admitted to hospital. Infants with chronic lung disease are at risk for subglottic stenosis and lower airway lesions including endobronchial granulations, bronchial stenosis, tracheomalacia, and bronchomalacia. Optimal treatment can be provided when these conditions are diagnosed. Flexible laryngoscopy can be used in intensive care units to evaluate the upper airway before or during extubation. It is particularly useful in evaluating the resolution of epiglottitis and in evaluating laryngeal injury following prolonged intubation or inhalation injury.

Bronchoscopy and bronchoalveolar lavage have proved to be particularly useful in diagnosing *Pneumocystis carinii* pneumonia in children with human immunodeficiency viral infection. Bronchoalveolar lavage is also useful in the diagnosis of pneumonia in children whose immune system is comprised by chemotherapy or other causes and in the evaluation of chronic radiographic infiltrates in children with chronic lung disease of unknown cause.

Complications of flexible laryngoscopy and bronchoscopy are generally infrequent. Minor complications occur in 2% or 3% and include epistaxis, transient bradycardia, and adverse reactions to anesthetic agents. Major complications, which include infection, pneumothorax, and laryngospasm, occur in about 0.4% of lower airway examinations. Death has been reported but is such an infrequent occurrence that it is rare even in large series.

Further applications and improvements in technique and instrumentation can only be expected as pediatric flexible bronchoscopy enters it second decade.

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Bone Marrow Transplantation for the Treatment of Genetic Disease

BONE marrow transplantation, the treatment of choice for various genetic diseases, may be efficacious for three categories of these diseases. The first is one in which the defect is expressed in the marrow stem cell, such as in patients with severe combined immunodeficiency disease. The disorder is the result of a congenital defect in lymphocytes in which the chances of surviving beyond 1 to 2 years of age without a bone marrow transplant are virtually zero, whereas 75% to 80% of children will be cured with its use. Until recently, only a relatively small number of these children could benefit from a bone marrow transplant because of the lack of histocompatible donors. With the development of techniques for depleting partially matched parental bone marrow of T cells, however, virtually every child with severe combined immunodeficiency now can be offered a curative bone marrow transplant. Other congenital marrow stem cell defects for which the procedure has been used include ß-thalassemia major, Wiskott-Aldrich disease, chronic granulomatous disease, and osteopetrosis.

The second category of genetic disease is one in which the defect is expressed in all tissues but involves mostly the marrow stem cell population. For example, adenosine deaminase deficiency and nucleoside phosphorylase deficiency, both of which result in severe combined immunodeficiency, and glucocerebrosidase deficiency, which results in Gaucher's disease, are disorders that principally involve bone marrow-derived lymphocytes and mononuclear phagocytes, respectively. Bone marrow transplantation with the successful replacement of these hematopoietic cells can significantly ameliorate the manifestations of these disorders.

The third category of genetic diseases for which bone marrow transplantation may be indicated includes those in which the defect is expressed in all tissues and there is substantial systemic disease involving many organs. The rationale for a bone marrow transplant in these patients is dependent on marrow-derived tissue histiocytes including Kupffer and Ito cells in the liver; Langerhans cells in the skin; microglia cells in the central nervous system (CNS); osteoclasts in the bones; and macrophages in the lung, spleen, lymph nodes, tonsils, and peritoneum. These marrow-derived cells of donor origin can repopulate affected organs in the recipient and provide a new source of enzyme activity. The lysosomal storage diseases are in this third category of genetic disease. More than 100 children with various lysosomal storage diseases have received a bone marrow transplant. Nearly half were children with Hurler's mucopolysaccharidosis, an autosomal recessive disorder affecting the enzyme ∂-L-iduronidase. Clinical manifestations of Hurler's syndrome include CNS deterioration, growth failure, joint disability, organomegaly, myocardial or cardiac valvular disease, upper airway obstruction with sleep apnea, corneal clouding, and hearing loss. Patients usually die within the first decade of life with mental retardation and severe cardiopulmonary disease. Bone marrow transplantation has been successful in lessening many of the manifestations of this disease and substantially altering its natural history. The dysmorphologic facial and body features are ameliorated, joint function is improved, and the cardiopulmonary abnormalities and organomegaly abate. In terms of the CNS disease, hydrocephalus does not progress or, in some patients, does not develop, and in more than half of the patients there has been no further deterioration in mental state. Whether the successful results of bone marrow transplantation in Hurler's syndrome will be repeated in other lysosomal storage disorders is unknown, and resolving this question will require carefully controlled clinical trials.

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Fetal Surgery

MOST prenatally diagnosed correctable malformations are best managed by appropriate medical and surgical therapy after maternal transport and planned delivery at term. A few simple anatomic abnormalities with predictable developmental consequences may be corrected before birth, however.

Fetal urethral obstruction interferes with the development of the fetal kidneys and lungs. Studies of animals have shown that obstruction produces renal dysplasia and pulmonary hypoplasia due to oligohydramnios, and these often fatal consequences can be ameliorated by decompression before birth. The natural history of fetal urinary tract obstruction has now been well documented by the sonographic follow-up of untreated cases, and selection criteria have been developed based on the ability to predict fetal renal function from fetal urine electrolyte levels and the sonographic appearance of the fetal kidneys. Although most fetuses do not require intervention, a fetus with bilateral hydronephrosis due to urethral obstruction in whom oligohydramnios develops may benefit from either early delivery and postnatal decompression if the lungs are mature or, if the lungs are immature, in utero decompression either by a catheter shunt placed percutaneously under sonographic guidance or by open fetal intervention to create a fetal vesicostomy. Several hundred fetuses have now been treated. It is clear that improvements in selection make it possible to avoid intervention in most cases and that decompression of an obstructed fetal urinary tract can prevent the development of fatal pulmonary hypoplasia.

Most babies born with congenital diaphragmatic hernia die of pulmonary insufficiency despite optimal postnatal care because their lungs are hypoplastic from intrauterine compression by herniated bowel. Despite more optimistic reports from children's referral centers, which see only the patients who survive transport, the mortality for diaphragmatic hernia diagnosed in utero is approximately 80% based on sonographic follow-up of more than 200 cases. There is a wide spectrum of severity, and some mildly affected children do well with conventional treatment. An algorithm for management has been presented that selects severely affected babies on the basis of a dilated stomach in the chest, mediastinal shift by a large volume of herniated viscera, and the development of polyhydramnios. For severe lesions detected before 24 weeks of gestation, repair before birth is possible. Extensive experimental work in fetal lambs and monkeys has shown that repair before birth is physiologically sound, technically feasible, and can be accomplished with safety for the mother and her reproductive capacity. The repair is technically difficult, and the first attempts in human fetuses failed because of an unanticipated problem with herniation of the fetal liver and kinking of the umbilical vein. The technical problems have proved surmountable, however, and several babies are now thriving after successful in utero repair.

Several other simple anatomic problems may be amenable to repair before birth. Although most cystic adenomatoid malformations of the lung can be corrected after birth, fetal hydrops can develop in fetuses, with large lesions causing significant compression of normal lungs and causing them to die in utero, a sequence that may be reversed by removing the abnormal pulmonary tissue. Some fetuses with large sacrococcygeal teratomas have high-output cardiac failure and hydrops and die in utero—again, a sequence that can be reversed only by interrupting the vascular steal either by occluding the vessels to the tumor or removing the tumor before birth. Simple obstructions to intracardiac blood flow may be amenable to fetal intervention, such as a recent attempt to dilate a stenotic aortic valve before birth. Some fetuses with heart block unrelated to anatomic abnormalities with ventricular rates slow enough (<45 beats per minute) to cause hydrops and fetal death may benefit from electrical pacing in utero. One of the most interesting observations to arise from experimental and now clinical fetal surgery is that the fetus heals without scarring or fibrosis. Unraveling the mechanisms of scarless healing in the fetus may allow therapies that improve healing after birth. Intervention for disfiguring but not life-threatening anomalies such as cleft lip and palate and craniofacial anomalies is not warranted at present, however. Fetal intervention is the logical culmination of advances in fetal diagnosis, and new applications are rapidly evolving.

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Predictors of the New Therapy for Jaundice

IN sick, premature, or severely jaundiced infants, the evaluation of risk for brain injury caused by bilirubin should include the measurement of arterial blood gas pressures, albumin level, and total serum bilirubin level. In a term infant with normal arterial pH and without hemolytic disease, the total binding capacity (in milligrams per deciliter) should probably not exceed the albumin concentration (in grams per deciliter) more than seven times. For example, if an infant has an albumin level of 3.4 grams per dl, an exchange transfusion should be done if the bilirubin level reaches 23.8 mg per dl (3.4 x 7). Using Système International (SI) units, the multiple should be 12: 34 grams per liter (albumin) x 12 = 408 µmol per liter (bilirubin). In very sick infants, the quality of albumin binding may be impaired, and a multiple of 5 to 6 times the albumin concentration might yield a more appropriate estimate of risk (9 to 10 x using SI units). Because the tissue deposition increases linearly with the hydrogen ion concentration, acidosis should be aggressively corrected in patients at high risk for bilirubin encephalopathy. This is particularly important in patients with respiratory acidosis because carbon dioxide rapidly equilibrates across the blood-brain barrier and increases the cerebral flow and bilirubin delivery to the brain.

For well, term babies without hemolysis or a serum bilirubin level well above 20 mg per dl, there is remarkably little evidence for adverse effects caused by bilirubin on intelligence quotient, neurologic function, or hearing. In fact, the diagnosis of neonatal jaundice as a "problem" may have negative consequences on maternal behavior and attitudes in the early, crucial months of infant development.

Nonetheless, the effects of hyperbilirubinemia in premature infants, who have increased bilirubin production compared with term infants, and term infants who have increased bilirubin production because they are sick or have hemolytic disease may be deleterious and different from those in well, term infants. Because of degradation of heme results in the equimolar production of carbon monoxide (CO) and bilirubin, the respiratory CO excretion rate, the end-tidal CO concentration, and the blood carboxyhemoglobin level can be used as indices of bilirubin production. Noninvasive technology currently exists for detecting an excessive production of bilirubin even before the development of jaundice.

Currently the two most widely used treatments of exaggerated neonatal hyperbilirubinemia are phototherapy and exchange transfusion, therapies which remove bilirubin that has already been produced. The suppression of bilirubin formation, however, is more logical preventive strategy, particularly when reserved for those patients who produce an excessive amount of the pigment. The first and rate-limiting step in the degradation of heme to bilirubin is catalyzed by the microsomal enzyme heme oxygenase. Numerous inhibitors of heme oxygenase have been identified, including tin, zinc, chromium, and manganese porphyrin complexes. Zinc protoporphyrin has recently been shown to inhibit bilirubin production and ameliorate hemolytic jaundice in nonhuman rhesus primates.

Two other pharmacologic strategies for ameliorating neonatal jaundice are also being considered. One involves bilirubin oxidase, a mitochrondrial enzyme that is capable of breaking down bilirubin to biliverdin and has been used in rodents with a congenital deficiency of glucuronyl transferase to interrupt the enterohepatic circulation of bilirubin. Another involves a traditional Chinese herbal concoction called *yin zhi huang*, which has been used in Asia to treat hepatitis and neonatal jaundice and has undergone some recent studies showing that it enhances bilirubin clearance from plasma and increases the conjugation of bilirubin by the liver.

Any new strategies to provide more specific therapies for infants at risk for dangerous neonatal jaundice should be combined with screening programs to identify infants who produce excessive amounts of bilirubin and who are at risk for potentially dangerous jaundice. Thus, infants who are at low risk for potentially dangerous neonatal jaundice could be spared an unnecessary use of laboratory testing and therapies.

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Interventional Catheterization for Congenital Cardiac Defects

HEART defects are the most common serious congenital anomalies. Interventional catheterization has had a major effect on the prognosis and costs of these defects. As many as 20% of structural cardiac defects can now be treated effectively in the cardiac catheterization laboratory, and this percentage could approach 40% in the near future. Therapy without thoracotomy, transfusion, or even an overnight stay in a hospital is now possible.

The list of potential uses of balloon valvuloplasty or angioplasty techniques is long and includes valvar and arterial pulmonic stenosis, aortic stenosis, coarctation, rheumatic mitral stenosis, and postoperative stenotic lesions. The greatest success and effect to date has been with valvar pulmonic stenosis. More than 800 balloon pulmonary valvuloplasties have been reported to an international registry. The transvalvar gradient was reduced greater than 70% with a mortality rate of 0.2%. The procedure was less effective in patients with a dysplastic pulmonary valve as is seen in Noonan's syndrome.

Survival rates and gradient reduction for balloon pulmonary valvuloplasty in infants with critical pulmonic stenosis have exceeded those of surgical valvotomy. Cyanotic heart defects with restricted pulmonary blood flow can also be palliated by balloon pulmonary valvotomy, obviating the need and problems associated with a Blalock-Taussig shunt or its variants. Many other stenotic lesions can be dilated, with current results approximating those of surgical outcome, but at lower cost financially and emotionally. The risks of restenosis of dilated arterial segments can be diminished with the use of intravascular stents.

Interventional procedures place great demands on the catheterization team and require experience and coordination. Complications may occur with valvuloplasty, including blood loss, obstruction of femoral vessels, vessel rupture, perforation, and valve destruction with insufficiency. The largest reported complication rate is about 12%, of which half were considered major. The incidence of complications is inversely related to a patient's age. Most complications occur in the very young where the necessity for operator experience and appropriate equipment size is the greatest. In some series, femoral vessel obstruction may occur in as many as 10% of angioplasty-treated children but usually can be treated medically. The overall mortality rate is, however, low (about 0.7%). Because of the potential serious complications, a surgical team should be available to minimize mortality. The economic effects of angioplasty-valvuloplasty procedures can be substantial with most interventional catheterizations costing 20% to 50% of a comparable operative procedure.

Catheter techniques to occlude pathologic or postoperative cardiac or great vessel communications have also become well established. Metallic coils or detachable balloons can be used to permanently occlude systemic-to-pulmonary artery collaterals, residual aorticopulmonary shunts, persistent left superior venae cavae, and arteriovenous malformations. The current success with patent ductus arteriosus occlusion devices will make their use the treatment of choice for older children with this defect. The demonstrated efficacy of the double umbrella or clamshell occlusion device for atrial septal defect and muscular ventricular septal defect should lead to prompt Food and Drug Administration approval and widespread clinical use. Additional interventional advances are on the horizon and will continue to improve the prospects for a near-normal quality of life for infants born with congenital heart disease. Cost savings will effectively allow for increased access to care within budgetary constraints.

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Diagnosis and Treatment of the Acquired Immunodeficiency Syndrome in Children

THE acquired immunodeficiency syndrome (AIDS) in children—symptomatic human immunodeficiency virus (HIV)—is becoming one of our nation's largest health problems; 3,213 cases of AIDS in children, ages 0 to 19, have been reported to the Centers for Disease Control (CDC) as of October 1, 1990. They represent about 2% of the total AIDS cases in the United States, now numbering more than 150,000. Further, there is considerable underreporting of pediatric AIDS because rigid criteria are necessary. It is estimated there may be as many as threefold more unreported pediatric AIDS cases in the U.S. It will soon be the fifth leading cause of death in children. Indeed, about 2,000 infants with HIV infection will be born to about 5,600 HIV-infected mothers annually in the U.S. Most of the cases are in the urban areas of populous states such as New York, New Jersey, Florida, Texas, and California.

Nearly all HIV-infected children have acquired their disease perinatally from their HIV-infected mothers. Transfusion-acquired cases make up only 11% of the total reported cases, and nearly all these patients were infected before April 1985, when the routine testing of blood products commenced. Mothers have become infected because of their own intravenous drug use (51%) or their sexual partner's seropositivity (38%), usually also a result of intravenous drug use. Most of these mothers are members of disadvantaged minorities, particularly African American (51%) or Hispanic (20%). (These groups make up 18% of the total U.S. population.) Thus, pediatric AIDS is now a disease of urban disadvantaged minority populations.

Infants and children with HIV characteristically get sick 6 to 18 months after infection; the first manifestation usually is recurrent respiratory tract infection, particularly bacterial or viral pneumonia. *Pneumocystis carinii* infection, candidiasis, persistent diarrhea, and poor growth are also noted early. Encephalopathy occurs in many children as the illness progresses, leading to intellectual and motor deterioration. Some older children get a characteristic pulmonary disorder, lymphoid interstitial pneumonitis, producing diffuse nodular or reticular pulmonary infiltrates and progressive dyspnea. The cause is not known.

TABLE 1.—*Indications for Testing for Human Immunodeficiency Virus (HIV) in Children and Adolescents*

Who could be tested

- Children of HIV-infected parents
- Children of "high-risk" parents—IV drug users, prostitutes, bisexuals, past residents of countries where HIV is endemic
- Children transfused between 1978 and April 1985, before HIV testing
- Children transfused after April 1985 in whom clinical or laboratory features of immunodeficiency develop
- Children with hemophilia who received clotting factor concentrates between 1978 and January 1985, before heat treatment
- Children whose parents request testing

Who should be tested

- Children with opportunistic infections suggestive of an immunodeficiency
- Children with evidence of T-cell immunodeficiency
- Children with recurrent infections and hypergammaglobulinemia (IgG plus IgM plus IgA levels > 18 grams per liter [> 1,800 mg per dl])
- Children with unexplained myopathy, nephritis, hepatitis, or progressive neurologic disease
- Children who are bone marrow or organ donors
- Children at "high risk" due to IV drug use, prostitution, or sex with high-risk persons

Ig = immunoglobulin, IV = intravenous

A physical examination may reveal prominent lymphadenopathy and hepatosplenomegaly. Parotitis may also be present. Other features such as growth failure are nonspecific. Immunologic abnormalities in HIV-infected infants and children include hypergammaglobulinemia; diminished antibody responses, CD4 cell (T-helper) depletion; reversal of the CD 4 to CD 8 (T-helper:T-suppressor) ratio; and poor results on functional tests of cellular immunity, such as proliferative responses to mitogens.

Table 1 suggests which infants and children may have HIV infection and should have an HIV-antibody test. A positive HIV-antibody test by screening enzyme-linked immunosorbent assay and confirmatory Western blot test generally indicates HIV infection in children older than 15 months.

Diagnosing HIV disease by antibody testing in infants is complicated by the presence of transplacental maternal HIV antibody in infants' circulation until as old as 15 months. The best way to establish a diagnosis in these infants is to identify HIV by culture of a patients' lymphocytes. The presence of HIV antigen in the plasma also is diagnostic, but it often is not present in early illness. The polymerase chain reaction to detect viral DNA promises to be a sensitive and specific test, but it is not routinely available.

Treatment is now available that will prolong life and prevent opportunistic infection in children with AIDS. *P carinii* pneumonia prophylaxis with the combination drug trimethoprim and sulfamethoxazole is recommended for all infants younger than 15 months with established HIV infection regardless of immunologic state, any older HIV-positive child with a DC4 lymphocyte count of less than 0.4×10^9 per liter (400 cells per µl), and any HIV-positive child with a previous *P carinii* infection. Trimethoprim-sulfamethoxazole is given as Bactrim or Septra, 150 mg per m^2 a day of trimethoprim component, in two divided doses three times a week, (Monday, Tuesday, and Wednesday).

The use of zidovudine (AZT) is recommended for children with CD4 counts of less than 0.5×10^9 per liter (500 cells per µl) or any child with CDC-defined AIDS. The usual initial dose is 180 mg per m^2 per dose every six hours, with dose reductions as needed because of hematologic or hepatic toxicities. Zidovudine is particularly valuable in reversing HIV encephalopathy. Side effects include neutropenia, anemia, and hepatic derangement.

The intravenous administration of immune globulin, 400 mg per kg every three to four weeks, is recommended if there is evidence of poor antibody function. All routine childhood immunizations should be given except that inactivated polio vaccine is given rather than oral polio vaccine. Despite these immunizations, immunity is not assured owing to deficient antibody responses. Appropriate antibiotics and antivirals are used promptly with each significant infection. Varicella-zoster immune globulin is used following varicella exposure. Other drugs such as dideoxyinosine (DDI), soluble CD4, and hyperimmune intravenous immune globulin are under investigation. The use of these therapies should improve survival, which is now about 38 months from time of diagnosis.

California has three centers for the treatment of pediatric AIDS: the San Francisco Bay Area (D. Wara, M.D. [415] 476-1736), the Los Angeles area (Y. Bryson, M.D. [213] 206-6369), and the San Diego area (S. Spector, M.D. [619] 543-6447). All are part of a national network of pediatric AIDS centers supported by the National Institutes of Health. Further information and referrals are available at these centers.

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Newborn Hemoglobinopathy Screening

IN February of 1990, California implemented hemoglobinopathy screening as part of the routine neonatal screening program. The hemoglobinopathy screening is done on all newborns regardless of race, creed, color, or ethnicity. The purpose of the screening is to identify infants with a clinically significant hemoglobinopathy and refer them to comprehensive-care sickle cell centers for follow-up support services. The Cooperative Study of Sickle Cell Disease, conducted by the Sickle Cell Branch of the National Institutes of Health, showed the effectiveness of parental education for the pediatric patients. Most deaths of children with sickle cell disease occurred between the ages of 1 and 3 years from serious infections. It has been reported that educating parents to take a temperature and identify a fever has decreased the mortality rate of young children with sickle cell anemia. Furthermore, the education of and counseling to parents on the importance of prophylactic penicillin have been demonstrated in national studies to decrease significantly the morbidity and mortality due to overwhelming infection or sepsis in infants with hemoglobin SS disease. Because sickle cell anemia occurs in 1 in 500 live births in the African-American population, primary care providers must be aware of the newborn screening process and participate actively in the referral and follow-up of these patients.

Primary physicians are notified by letter or a telephone call from the newborn screening nurse coordinator in the area. The patient's name, date of birth, mother's name and address, and preliminary diagnosis are provided. When a patient is seen for the initial visit, it is strongly recommended that the primary physician begin prophylactic penicillin therapy, inform the family of the comprehensive care sickle cell center in the area and encourage them to call for an appointment, and call the sickle cell center and make a referral.

The role of comprehensive-care sickle cell centers in the management of clinically significant hemogloinopathies in newborns includes medical intervention and consultation by a pediatric hematologist with specific training in hemoglobinopathies; a nurse specialist to provide clinical assessment and parental education; a master's level social worker or equivalent family therapist to discuss psychosocial issues or needs that may affect the child or family; and within the comprehensive care setting, other health professionals who are available for consultation from various specialty areas to meet patients' needs.

In addition to identifying sickle cell disease, the newborn screening program will detect variant forms of other significant hemoglobinopathies as well as heterozygote hemoglobin disorders such as AS, AC, and AD. These traits appear to be harmless and do not cause serious health problems. Combination hemoglobinopathy-thalassemia syndromes will also be detected by the newborn screening program. In California, all infants having these traits are referred to primary care physicians by a letter from the Department of Health Services, Newborn Screening Section. This letter also lists the names of sickle cell counseling centers in the family's area that can provide information on the hemoglobin trait the child has by the authorization code assigned by the Newborn Screening Section. The physicians again play an important role in providing initial information and counseling and by referring such families to comprehensive-care sickle cell centers for more in-depth education and counseling.

Full participation by primary care providers in this program is essential for its success and should result in optimal care for children with substantial hemoglobinopathies.

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Steroid Therapy for Bacterial Meningitis

THE idea that glucocorticoids might prove to be a useful adjunctive therapy for meningitis has been in the literature for more then 30 years. The choices of experimental design, the choice of steroids administered, the choice of dose, and the lack of clarity about which outcomes to measure all stood in the way of demonstrating a beneficial effect. During the past five years two separate lines of investigation have provided much new information in this area.

The development of an excellent rabbit model for purulent meningitis allowed several groups of investigators to work out the pathophysiologic events in bacterial meningitis. Bacteria enter the central nervous system, multiply rapidly, and liberate cell wall products (endotoxin, teichoic acid). These inflammatory agents in turn stimulate host cells to produce various potent cytokines (tumor necrosis factor, interleukin, and others). The inflammatory cascade results in a serious pathologic disorder including brain edema, increased intracranial pressure, decreased cerebral perfusion, a loss of autoregulation, and, ultimately, permanent brain damage. Rabbits are well suited to the study of various forms of therapy, including the use of anti-inflammatory drugs. It has been clearly shown that in rabbits the use of dexamethasone given simultaneously or before antimicrobials in cases of *Hemophilus influenzae* meningitis abolishes or greatly ameliorates the profound inflammatory response and other untoward consequences of infection that cause most of the residual damage. Not all steroids have similar anti-inflammatory action. Methylprednisolone, for example, fails in several important respects.

At the same time, the use of dexamethasone has been evaluated in human studies, mostly in children with *H influenzae* meningitis. The pathophysiologic studies had results similar to those found in rabbits. Children given dexamethasone had fewer signs of inflammation. Adverse effects of dexamethasone use appear to be limited to a small incidence (1.5%) of gastrointestinal bleeding. Well-controlled outcome studies in several hundred patients failed to show the effects of dexamethasone therapy on mortality, which was low in this series. The early use of the drug, however, along with antimicrobial therapy was associated with a distinctly lower incidence of bilateral moderate or greater hearing loss compared with results in patients treated with antimicrobials or a placebo. Confounding the results was the use of cefuroxime as the antibiotic in portions of the study. This agent is no longer recommended for the treatment of bacterial meningitis due to its delay in sterilizing the cerebrospinal fluid of patients.

The immediate application of the new knowledge to clinical practice is still somewhat controversial. Multicenter studies including larger numbers of children in the United States and abroad are in progress. Larger numbers will be of great value in further evaluating both the beneficial effects of adding steroids to the treatment regimen and further exploring any adverse effects.

As we await the outcome of these expanded trials, the American Academy of Pediatrics has recommended "individual consideration of dexamethasone for bacterial meningitis in infants and children 2 months of age and older after the physician has weighed benefits and possible risks." The only published regimen for dexamethasone is 0.6 mg per kg of body weight per day in four divided doses given intravenously for four days beginning with or just before the first dose of antibiotic therapy. The use of dexamethasone in bacterial meningitis due to organisms other than *H influenzae* is not established, but it may be reasonable to use the drug in a child with purulent meningitis in whom the bacterial cause is not yet confirmed. There is no reason to use dexamethasone in patients with aseptic meningitis. The use of steroids in adult patients should await the outcome of further clinical trials. Another important area awaiting clinical trials is the use of steroids in neonatal meningitis.

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Biotechnology and the American Agricultural Industry

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To meet the needs of a rapidly growing population and minimize the toxic influences of traditional farming practices on the environment, the American agricultural industry has applied molecular technology to the development of food crops and livestock. By placing genes specific for highly desirable phenotypes into the DNA of plants, animals, and bacteria, farmers have increased crop and livestock survival, enhanced the nutritional quality of foods, increased industry productivity, and reduced the need for toxic pesticides and herbicides. However, introduction of genetically modified foods into the marketplace has raised a spectrum of public health issues. Physicians, as the most proximal scientific resource for most individuals, are uniquely positioned to address patient concerns regarding the safety of genetically altered foods. This report provides an overview of the inherent risks and benefits of "agrogenetics" and offers a series of recommendations designed to promote the education of the medical community and dispel public misconception regarding genetic manipulation.

Agricultural Biotechnology and the Physician

RECOMBINANT-based proteins and genetically engineered microorganisms have been applied to the agricultural industry to improve the food supply, increase industry productivity, and reduce the adverse effects of agricultural practices on the environment. All of the major food groups, which include fruits, vegetables, dairy, meats, and grains, are targets for modification by gene replacement or manipulation.[1,2] By 1995, many of these food products will be available on grocery store shelves and as experience indicates, consumers *will* be questioning the safety of these foods. To ensure that the remarkable advances in agriculture and subsequent improvement in public health are not delayed, these concerns of the public must be addressed. Since the physician represents, in most cases, the only scientifically trained professional in regular contact with the public, it is logical that individuals will turn to their physicians with questions about the safety of genetically modified foods. Therefore, clinicians are in a unique position to influence the acceptance of genetically modified foods by addressing patient fears about the impact of biotechnology on daily life. To maximize their influence, physicians must understand the process of genetic engineering not only as it applies to medicine, but as it applies to public health.

Agricultural Genetics

The genomes of plants and animals have been modified through selective breeding for centuries. However, today's understanding of molecular biology allows the agricultural scientist to select the gene that translates into a desirable phenotype and place that gene into the genome of a second organism. Rather than depending on "natural mutation," these scientists directly manipulate DNA to rapidly improve specific plant, animal, or bacterial characteristics.

Prior to molecular technology, plant and animal pheno-

From the Council on Scientific Affairs, American Medical Association, Chicago, Ill.

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This report is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all the facts and circumstances involved in an individual case and are subject to change as scientific knowledge and technology advance and patterns of practice evolve. This report reflects the views of scientific literature as of June 1990.

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types changed through evolution because of natural gene mutation and arrangement. Although many of the phenotypically altered plants and animals may not have survived the natural selection process, human intervention has allowed the propagation of those "genetic mutants" exhibiting desirable characteristics. Thus, the tremendous variety of foods available today results from the combined effects of natural genetic variability and direct human intervention. The techniques that constitute the basis of molecular biology (directed gene mutations and gene recombination) are the same mechanisms underlying evolution. Therefore, the application of recombinant DNA technology to agriculture is primarily a refinement of traditional plant genetics and breeding practices.[1,3] This concept is critical to the understanding of gene manipulation as it applies to agriculture.

Recombinant DNA Technology

The manipulation of DNA by recombinant techniques underlies the molecular advances in both medical and agricultural biotechnology.[1,4-6] *Recombinant DNA* is a term that describes the joining or recombining of two or more pieces of DNA, one of which might be the gene fragment of interest and the other a "vector" DNA. DNA derived from a bacterium, virus, or plant or animal cell can be recombined with the DNA from bacteriophage, retrovirus, yeast, or plasmid vector. The "recombinant vector DNA" is then inserted, by chemical or physical means, into a mammalian, plant, or bacterial cell. The gene of interest may then integrate randomly within the host cell DNA or remain as episomal DNA capable of replicating independent of the host. On rare occasions, the gene may combine with and replace or inactivate the resident gene (a process called *homologous recombination*). Both integration and independent replication represent stable mechanisms to express a gene of interest in a foreign cell. The foreign DNA does not travel within the host cell genome; therefore, minimal risk of inducing pathogenic mutations or gene rearrangement exists.[1]

Often an antibiotic resistance gene is incorporated into the vector DNA so that the integration and expression of the foreign DNA can be monitored. If integration of the foreign DNA is successful, only those plant cells expressing the resistance gene will survive when treated with the appropriate antibiotic. Many antibiotics are under study as potential selectable markers for both consumable and nonconsumable crops, including kanamycin, chloramphenicol, gentamycin, and trimethoprim.[3,7] Before these markers can be generally introduced into consumable products, the likelihood of inducing antibiotic resistance in humans and livestock will require study. Evidence to date suggests that the resistance markers are *not* transposable between the ingested plant material and potentially pathogenic microorganisms, although further evaluation is indicated. The use of antibiotic-resistance markers in food crops is currently under advisory within the Food and Drug Administration (FDA).

When the foreign DNA replicates independently of the host cell DNA (a process that occurs in bacterial systems only), many copies of the gene fragment of interest are synthesized. In this manner DNA is cloned. When the foreign DNA integrates into the host cell DNA, the gene fragment may be expressed and subsequently alter the host cell phenotype and function. Alternatively, the host cell can be externally triggered to produce large quantities of the foreign gene product.[1,8] A variation in the latter mechanism is the manner in which recombinant protein therapeutics are manufactured.[4,5,9] Using these recombinant DNA techniques, the agricultural industry produces large quantities of desired proteins such as hormones, essential plant and animal nutrients, and peptide vaccines.

An exciting new development in recombinant DNA technology is the creation of transgenic organisms. A *transgenic organism* is one in which a gene has been physically inserted into the nucleus of an embryonic, stem, or germ cell such that the gene is present in the somatic cells of the organism. The genes may be placed into the nucleus of the cell by a number of mechanisms including chemically mediated transfection, microinjection, electroporation, microballistic projectiles, and vector- (plasmid, viral, or bacterial) mediated transfer. The function of the transfected DNA in the genome of the "stem" or "seed" cell may be to give the organism a phenotype that it did not previously express, or it may be to interfere with the expression of an endogenous gene. The latter situation can be accomplished by synthesizing or constructing a fragment of the targeted gene in the opposite or antisense orientation. During transcription, an "antisense" messenger RNA is synthesized that complexes with the host "sense" messenger RNA. The duplex is quickly degraded so that no sense message is available for translation into protein. When gene expression can be targeted to specific tissues, so that transcription is tissue selective, the utility of transgenic organisms will be greatly enhanced. Tissue-specific gene expression is well established in plants but remains experimental in higher organisms.

Genetically Engineered Plants

Agricultural genetics have been most successfully applied to the increased production and protection of crop plants. Currently, genetically engineered plants have been developed that can resist disease, degrade herbicides, and tolerate long-term storage.[10-14] Although successful, genetic modification of plants has been limited by the inability to mechanically transfer foreign DNA into the appropriate cells of the plant and still maintain

Food/Feed Plants That Have Been Genetically Modified to Resist or Tolerate Herbicides, Insects, and Virus[1,2]

Tomato*
Potato
Celery
Tobacco†
Carrot
Walnut
Lotus
Poplar
Alfalfa
Peas
Lettuce
Sunflower
Rapeseed oil‡
Bean
Cauliflower
Orchard grass
White clover
Soybean
Cotton
Cabbage
Rice
Broccoli
Sugar beet
Horseradish
Pear
Cucumber
Asparagus
Apple
Corn§
Alfalfa
Rye

*Also genetically engineered for reduced spoilage.[2,15,16]
†Also genetically engineered for antibody production.[9]
‡Also genetically engineered for decreased saturated fatty acids.[2,13]
§Also genetically engineered for increased levels of specific amino acids.[2,24]

plant fertility. Therefore, the most successful approach to the creation of transgenic plants has been to clone the gene of interest into the bacterium *Agrobacterium tumefaciens*, a plant pathogen that colonizes many different crop plants. During colonization, the bacterial plasmic DNA is randomly transferred into the plant chromosome.[3] For *Agrobacterium*-mediated gene transfer, the bacterial gene fragments responsible for pathogenicity are removed. Because the plant cell DNA does not contain the properly oriented regulatory machinery to transcribe the bacterial DNA, only the foreign gene, carried on the bacterial vector, is expressed, and, therefore, bacterial gene expression that may have posted a threat to human or animal health is unlikely to occur.[1,15,16] As only certain plants (primarily the dicotyledons) are susceptible to colonization by the *A tumefaciens* bacteria, other means of DNA delivery are under study. The most promising development involves the high-velocity ballistic transfer of DNA, in which DNA-coated tungsten particles are "shot" at extreme velocity into intact plant cells.[1,15] In this manner, the DNA is able to penetrate the complex plant cell membrane and nuclear integration is probable.

Examples of Genetically Modified Plants

By 1965, a variety of transgenic plants are scheduled by industry to be available to the consumer, including tomatoes genetically altered for increased storage, corn modified to provide increased nutrient value to livestock and increased digestibility, plants capable of *degrading* herbicides, and crops carrying genes or genetically modified bacteria that provide for resistance to insects, virus, frost, and changes in temperature. Herbicide-*resistant* crops such as corn, potatoes, rice, soybeans, lettuce, and cole (broccoli and cauliflower) are expected to be on the grocery store shelves, as well as virus-resistant tomatoes, potatoes, alfalfa, melons, soybeans, strawberries, sugar beets, and cole plants (Table).

One mechanism for inducing *pesticide resistance* in plants is to transfer the gene for the delta endotoxin originating from select *Bacillus thuringiensis* subspecies (the Bt protein).[1,17,18] When ingested by an insect, the recombinant endotoxin is converted to an active poison that disrupts ion transport of cell membranes in the gut of pests.[17] The toxin is lethal for the larvae of moth, butterfly, beetle, and certain fly species and will soon be available in a modified form that will increase host range. The toxin produces no apparent toxic effects in mammals, fish, birds, most plants, or beneficial insects.[15,19] In fact, the Bt endotoxin has been used in a pesticide spray form for the past 30 years. One public health concern is whether the concentration of the Bt protein in the transgenic plant exceeds the concentration of the exogenously applied toxin following plant processing. Whereas the toxin contained within the pesticide spray may degrade or wash away, minimizing human exposure, the protein produced by the plant may be constitutively present in high concentrations. To circumvent this issue, Bt gene expression is generally limited to a single, highly susceptible developmental stage in the plant's life cycle (before maturation and harvest occur). A second concern that will require continued monitoring is the safety of any change in the chemical structure of the toxin that results from protein modification subsequently to gene manipulation.

Herbicide-Resistant Plants

Certain plants have been engineered to withstand commonly used herbicides. The herbicides destroy weeds by inactivating an essential metabolic enzyme that is present in the targeted weeds as well as the crop plant.[1,20] To avoid destruction, the genetically modified crop plants have been engineered to produce an enzyme less sensitive to the herbicide, produce greater quantities of endogenous enzyme, or produce an enzyme that inactivates the herbicide.[18] Although critics contend that the use of herbicide-resistant plants will result in greater application of herbicides, the agricultural industry has developed potent, broad-spectrum herbicides that produce few toxic effects and exhibit low soil mobility and increased rates of degradation.[15] These biodegradable herbicides are predicted to reduce industry use of the environmentally destructive chemicals that exhibit narrow specificity and require more frequent application.

Antisense Tomatoes

Tomatoes have been transfected with the "antisense" gene responsible for polygalacturonase, which solubilizes pectin.[1,16,21] Since pectin degradation increases fruit ripening and decreases fruit shelf life, preventing the translation of the message (by having the antisense message present) for polygalacturonase will retard fruit ripening and increase prepurchase and postpurchase fruit shelf life.

Plants Resistant to Virus Infection

Botanical viruses have the capacity to devastate entire food crops, including corn, wheat, rice, soybeans, and potatoes. To combat plant viral disease, virally resistant plants have been developed by introducing the gene that encodes the coat protein of the viral pathogen into the genome of the plant. The expression of the coat protein retards subsequent viral infection and/or replication and spread.[1,15] Viral resistance will improve crop quality and yield and decrease the need for insecticides directed against vectors that spread the virus.[1] Studies indicate that the coat protein will be present in levels of 0.01% to 0.5% of total plant protein, which is 5000-fold less than the amount of viral protein found in the consumable plants in which virus infection is now endemic. Therefore, the genetic insertion of viral coat protein genes into consumable plants is not expected to present a health risk for humans and livestock.[15,18]

Although consumer interest exists for foods that have increased sensory value and increased nutrition, *agricultural economics* as well as scientific complexity has dictated that the emphasis of agro-biotechnology be on control of weeds, insects, and plant disease.[15,16,19] Plant characteristics such as flavor, color, and nutrition are often governed by multiple complex gene sets, making genetic manipulation virtually impossible with current technology. Beyond the financial implications that this barrier presents, health concerns exist. Each genetic alteration in a plant crop increases the potential for complications resulting in the activation of unwanted, possibly toxin-producing genes and the potential loss of genes expressing desirable traits.[16,18,22]

However, certain nutritionally enhanced crops have been developed. Strawberries were found to contain low levels of ellagic acid, a cancer-protective agent that inhibits polycyclic aromatic hydrocarbons, nitrosamines, aflatoxin, and aromatic amines.[16] Agricultural scientists are currently cloning the gene in the hope of inducing high levels of ellagic acid production in the natural host or in a genetically modified organism. Similarly, the rapeseed plant from which consumable canola oil is derived has been genetically engineered to contain increased unsaturated fatty acids.[16]

Regulation of Foods Derived by Genetic Modification

Despite the prediction that genetically altered food crops will be available to the consumer within the next five years, controversy exists concerning the appropriate regulatory and educational machinery required to evaluate these products. Both the Biotechnology Office of the FDA and the International Food Biotechnology Council state that existing regulatory measures should be "kept in place, strengthened with the progress of science, and adjusted as needed in their application to meet the spectrum of situations posed by new methods of genetic modification."[1] The concern is that additional regulations will significantly impede the development and commercialization of important biotechnologies. However, each organization recognizes the need for strict regulation of those genetically engineered food products that derive from genetically unique or pathogenic source or those that contain genetic information for proteins to which humans have not been previously exposed.

Both the FDA and the International Food Biotechnology Council consider genetically engineered plants and microorganisms to be as safe as those derived from the traditional means of genetic manipulation, which include directed mutation, selection, and breeding, but necessarily outside of agency oversight.[23] The genetically modified food crops currently under field test are identified as low risk to human health because of the detailed knowledge of the introduced DNA, an extensive understanding of the functions of the gene product, and the assurance of a high level of biological or physical containment until field tests are completed.[23]

The tremendous advances in bioagriculture will soon bring genetically modified plants to the consumer. Just as a need exists for highly sensitive analysis or purified recombinant protein, so does a need exist for the evaluation of the potential adverse health effects of the expression of foreign protein in the traditional foods. The necessity for regulatory agencies to include these requirements in approval guidelines is imperative but should not prohibit the rapid assimilation of genetically derived foods and food additives that meet the standards of existing regulations.

Livestock: Applications of Recombinant DNA Technology

Unlike the dramatic strides that have taken place in the genetic engineering of food crops, the genetic improvement of livestock remains largely in the developmental stages. However, the advances that are available will improve the economic efficiency of livestock agriculture and provide increased nutritional value to foods originating from farm animals. The advances in animal agriculture include (1) the introduction of recombinant-based animal vaccines; (2) monoclonal antibody- and DNA-based detection kits that allow early detection and treatment of life-threatening disease in farm animals; (3) genetically altered feed crops that contain increased amounts of essential amino acids, including lysine and methionine; (4) recombinant DNA-derived proteins that can manipulate animal physiology and metabolic activity, such as milk production in dairy cattle and fat production by swine; and (5) the creation of transgenic farm animals for the purpose of controlled germ line selection and generation of high-production livestock herds.[24-26]

For the consumer, these improvements will translate into nutritionally improved meats and other animal byproducts, decreases in food prices through better farm management and decreased animal disease, and a secure food supply for the future. Many of the advances in livestock agriculture have been implemented without significant impediment, including the cloning of animal embryos, the use of recombinant DNA to detect and treat disease, and the use of genetic engineering to modify feed crops. However, the presence of recombinant DNA-derived genes and proteins in meat, dairy, and poultry food products has provoked concern.[27] The recombinant-based proteins in these foods have originated from genetically modified microorganisms or from the expression of a transgene incorporated into the germ line of the animal. In either case, the safety issues are similar to those that must be addressed before genetically modified plant crops can be introduced into the marketplace: (1) Has human exposure to this protein been proved safe? (2) Is the protein chemically modified or present in concentrations exceeding those proved to be safe?

Transgenic Livestock

Similar to the genetic selection of plant crops, the germline genetic improvement of livestock has been occurring for decades by the traditional practices of selective breeding. Transgenic animals are created in much the same way as transgenic plants. A gene of interest is inserted by microinjection or retrovirus-mediated gene transfer into the nucleus of the oocyte or the embryo which is then implanted into a hormonally prepared female. Expression of the transgene is evaluated in the subsequent progeny.

With current technology, the DNA introduced into the embryonic cells randomly inserts into the chromosomal DNA. In the near future, homologous recombination (targeted gene insertion in which the gene of interest either replaces or inactivates the homologous host gene) will be possible, allowing greater control over tissue-specific and developmentally regulated gene expression. Transgenes are often used to introduce new or enhance native animal characteristics in a tissue- or developmentally specific manner.[24] The most likely candidates for agriculturally important transgenes are growth hormones, metabolic enzymes, and disease-resistant genes.

The transgene technology has also been exploited in the agricultural industry for the production of therapeutic proteins. Human genes have been incorporated into the germ line of cows, sheep, rabbits, and mice in an effort to produce mass quantities of human protein in animal milk, ie, coagulation factor IX, tissue plasminogen activator, and interleukin 2.[28,29] The extremely low efficiency of transfection, low levels of gene expression, high cost to maintain the animals throughout their reproductive lives, and high cost of protein extraction have hampered this approach.[24,25] Therefore, it is unlikely that these animal bioreactors will replace genetically modified bacteria as the source of recombinant-derived therapeutics.

Examples of Recombinant Application to Livestock Agriculture

Transgenic Pigs

The most technically successful application of the transgene technology to domestic livestock has been the creation of the transgenic pig. These pigs carry the transgenes for various species-specific growth hormones, including human, bovine, rat, and swine somatotropins.[24,25] Transgenic pigs were created in the hope of improving the economics of the swine industry by increasing animal weight while reducing meat fat content.[25] As hoped, pigs expressing the somatotropin transgene experienced significant increases in daily weight gain and feed efficiency and significant decreases in the presence of subcutaneous fat. However, severe adverse reactions directly attributable to the chronic expression of the growth hormones were also observed, including gastric ulcers, degenerative joint disease, and infertility.[24,25] Similar adverse effects of long-term exposure to growth hormone have been observed in mice and sheep.[30, 31] These studies demonstrate that expression of growth hormone transgenes increases the nutritional value of meat products, but only at the expense of animal health. Therefore, studies addressing the potential human safety issues and those that continue to address animal health are necessary before transgenic animals as a nutritionally improved meat source will reach the consumer marketplace.

Recombinant Growth Hormone

An alternative to the creation of transgenic animals for increasing feed efficiency and animal productivity is the repeated exposure of animals to exogenous growth hormone during defined periods of intense metabolic activity. Preliminary studies indicate that pigs exposed to exogenous growth hormone during various growth stages, including lactation, exhibited meat-to-fat ratios similar to those observed in the transgenic animals but did not manifest the serious side effects.[32-35] However, the safety of human ingestion of meats containing large quantities of nonhuman growth hormone has been addressed in only a limited number of studies.[36-38] Exogenous growth hormone has also been used to increase the production of milk in dairy cows. Cows injected during peak lactation times with pituitary bovine somatotropin (bST) demonstrated a greater than 10% increase in milk yield.[39-44] However, the extraction and purification of the protein was expensive and required 200 cow pituitary glands for the production of a single injection of bST.[40] Therefore, several companies developed a recombinant bST (rbST) that could be produced in mass quantity at low cost (approximately $0.50 to $1 per injection).[40] The FDA has approved the field test of rbST, and subsequent studies indicate that daily injections of dairy cows with rbST increased milk production by 8% to 40%, while increasing animal feed intake by only 15%.[24,25,40,41,45-53]

Animal safety studies completed to date indicate that daily injections of lactating cows with rbST do not appear to cause severe adverse health reactions in the animals or in calves born to cows receiving rbST.[39,41,45,48-50,52,54-58] However, treated animals entered a prolonged period of negative energy balance and lost weight as a result of the hormone-induced increase in the conversion of body fat into milk. Although several reports demonstrated that rbST-treated animals exhibited increased susceptibility to mastitis, heat intolerance, multiple births, and decreased reproductive capabilities, these reports have been largely discounted due to the small trial sizes involved.[54] The findings do imply, however, that animals treated with rbST require consistent, high-quality care to avoid complications during the extended periods of negative energy balance. The long-term effects of rbST on cows have not been evaluated. However, dairy cows experience an average of only three lactations before sacrifice for meat production. Therefore, those studies evaluating the influence of rbST on the health of the animal over a period of three lactations cover the agriculturally productive life of the dairy animal.[59,60]

Recombinant Growth Hormone/Human Safety

Of critical concern to the consumer is whether the milk derived from rbST-treated cows is safe for human consumption. All studies to date indicate that the composition of the milk produced from an rbST-treated cow is similar to that of the milk produced from control cows. Native bST is found in the milk of all cows, and the total levels of bST (recombinant plus native) in the milk of cows treated with the hormone remain similar to the levels of native bST detected in control cows. Increases in the levels of unsaturated fatty acids, insulinlike growth factor, and milk proteins have been reported; however, the increases in levels of milk proteins are considered statistically insignificant.[46,50,53,61,62] No information is available on the direct effect of the increases in butterfat and insulinlike growth factor on nutrition and human health. However, indirect evidence of human safety derives from the finding that breast-fed infants are exposed to chemically identical human insulinlike growth factor that is present at high concentrations in human milk.[61] Further studies will be required to determine whether ingestion of higher than normal concentrations of bovine insulinlike growth factor is safe for children, adolescents, and adults.

The rbST is chemically and structurally similar to the native bovine somatotropin; the recombinant protein contains an amino terminal methionine or an 8- or 13-amino acid linker sequence required for cloning the recombinant protein in bacteria.[39,63-67] No immune response directed against the rbST linker amino acids has yet been reported. However, no detection methods are available that distinguish rbST from native bST. Therefore, the percentage of the rbST in the hormonally treated animal milk is unknown. Monoclonal antibodies have been prepared against the recombinant *human* somatotropin that distinguish the recombinant from the native forms.[68] The antigenicity appears to reside in the amino terminal methionine of the human recombinant protein.[68,69] Therefore, an antibody-based detection assay could be devised to determine the percentage of recombinant vs native bST present in the milk from rbST-treated animals.

In addition to immunogenicity, the ability of rbST to stimulate human somatogenic and lactogenic receptors has been questioned. Although stretches of amino acid sequence within the native bST protein are nearly identical to the human somatotropin, critical differences exist in the amino acid domains responsible for receptor binding.[63-65] Bovine somatotropin exhibits only low-level binding affinity for the human somatotropin receptor and does not induce significant metabolic activity. The finding that bST had no effect when injected into children suffering from growth hormone deficiencies supports this finding.[39] Because rbST is a protein, enzymes in the digestive tract will cleave the protein into many fragments. The tryptic peptide map of rbST indicates that the receptor-binding domain of the protein is cleaved into no fewer than four fragments, the longest of which is only nine amino acids long. Therefore, even if the rbST or digestive fragments were able to reach the circulation following ingestion of the milk, the recombinant protein fragments would not be expected to exhibit any deleterious activity. The potential immunogenicity of the peptide fragments remains to be determined.

Based on the following criteria, the FDA has approved human consumption of milk from rbST-treated cows:

1. BST is a protein, not a steroid hormone, and is therefore easily broken down in the digestive tract.
2. Because BST differs structurally from the human counterpart, the bovine hormone has no effect on human growth hormone receptors. This has been shown in vitro and in vivo when bovine somatotropin was evaluated in children for treatment of dwarfism.
3. Native somatotropin exists in bovine milk and therefore human consumption of bovine somatotropin is not new.[39,70]

The creation of transgenic animals and the development of recombinant growth hormones represent the two most visible and controversial applications of genetic engineering to the livestock agricultural industry, primarily because of the potential impact these developments may have on human health. In fact, rbST is the first economically important product of agricultural biotechnology to be ready to enter the marketplace. The success of this product may lead the way for other agrobiotechnology products, both plant and livestock, that will undoubtedly benefit a greater proportion of the population than will rbST. It is hoped that the economic, political, and social obstacles impeding the introduction of rbST will not retard the development and commercialization of equally or more beneficial advances in agricultural biotechnology.

Other Advances in Livestock Biotechnology

Other equally exciting advances in agricultural biotechnology exist, although with less potential impact on human health.

Embryo Cloning

The goal of current breeding practices is to selectively enhance the desirable characteristics of animals, including productivity and food nutrition. Therefore, progeny of highly desirable matings are extremely valuable. To increase the numbers of these valuable progeny, embryos from desired matings can be sex-selected and then split to produce twins or greater multiples, effectively doubling the number of prime offspring. A kit is now available for farmers to perform this procedure in vitro on the farm.[26]

Disease Detection and Prevention

Annual agricultural economic losses due to animal death, morbidity, and disease have approached $5 billion.[24] Therefore, applications of recombinant DNA technology to the development of vaccines and monoclonal antibody diagnostic kits have received great attention. A recombinant DNA-based vaccine is now available for the treatment of foot and mouth disease and pseudorabies in calves and swine, respectively, and monoclonal antibody-based kits are available for detection of enteric colibacillosis.[24,71]

Rumen Bacteria

Rumen bacteria (primarily *Bacteroides* and *Clostridia*) exist in the gut of the ruminating animals in a symbiotic relationship. If appropriate delivery systems could be devised, the bacteria could be genetically modified to provide antibiotic resistance, facilitate digestibility, produce essential amino acids, improve rumen fermentation, suppress the growth of undesirable or pathogenic organisms, and synthesize hormones that would increase the metabolic efficiency of the animals.[24,72]

Feed Crops

Genetic modification of animal feed crops is an alternative means to prevent disease and enhance digestion. Under field trial are feed crops that have been genetically engineered to provide increased levels of essential amino acids, such as lysine in corn and tryptophan in grain, reducing the need for expensive supplementation.[1,24] With the recent association of human eosinophilic connective-tissue disease with tryptophan ingestion, the safety of these feeds for indirect human consumption will have to be addressed.[73]

Summary and Recommendations

The application of recombinant DNA technology to agriculture is the natural extension of the sophisticated agricultural practices that have been refined over the past hundred years and more. Manipulating the genomes of microorganisms, plants, and animals will provide this country with the means to streamline the agricultural industry, reduce waste, control pollution, enhance the safety and nutrition of foods, and ensure that an adequate food supply exists to support the expected rise in the world population for the foreseeable future. However, appropriate regulations are needed to ensure that safety issues are addressed, especially those impacting on public health, while not overly restricting the application of recombinant DNA technology. The consumer must be educated regarding the real and potential risks inherent in recombinant DNA biotechnology as it applies to daily life. By understanding the risks and the great benefits of agricultural biotechnology, physicians may play an important leadership role, help to allay fear, and facilitate biotechnology innovation.

Therefore, the Council on Scientific Affairs recommends that the American Medical Association:

1. Endorse or implement programs that will convince the public and government officials that genetic manipulation is not inherently hazardous and that the health and economic benefits of recombinant DNA technology greatly exceed any risk posed to society.

2. Where necessary, urge Congress and federal regulatory agencies to develop appropriate guidelines that will not impede the progress of agricultural biotechnology, yet

will ensure that adequate safety precautions are enforced.

3. Encourage and assist state medical societies to coordinate programs that will educate physicians in recombinant DNA technology as it applies to public health, such that the physician may respond to patient query and concern.

4. Encourage physicians, through their state medical societies, to be public spokespersons for those agricultural biotechnologies that will benefit public health.

5. Actively participate in the development of national programs to educate the public about the benefits of agricultural biotechnology.

Glossary

Amino acids.- The building blocks of proteins. There are 20 common amino acids; they are joined together in a strictly ordered "string" that determines the character of each protein.

Amplification.- The production of many copies of a region of DNA.

Antigen.- Any molecule whose entry into an organism provokes synthesis of an antibody (immunoglobulin).

Antisense [RNA].- Transcription of a "nonsense" RNA message complementary to the "sense" messenger RNA. Antisense RNA is derived from a gene constructed in the 3'-5' or opposite orientation.

Bacteriophage (phage).- A virus that infects a bacterial cell. Phage consist of a core of genetic material (DNA or RNA) carrying the particle's genetic information that is surrounded by a protein coat or capsule. When a phage infects a host cell, the cell machinery that manufactures protein in response to genetically encoded instructions is comandeered by the phage and used to produce offspring phage. The lambda bacteriophage is frequently used as a vector in recombinant gene experiments.

Bioremediation.- Degradation of industrial waste by genetically modified microorganisms.

Biotechnology.- The collection of industrial processes that involve the use of biological systems. For some industries, these processes involve the use of genetically engineered microorganisms.

Chromosome.- The location of hereditary (genetic) material within the cell. This hereditary material is packaged in the form of a very long, double-stranded molecule of DNA surrounded by and complexed with several different forms of protein. Genes are found arranged in a linear sequence along chromosomes, as is also a large amount of DNA of unknown function.

Clone.- A group of genetically identical cells or organisms asexually descended from a common ancestor. All cells in the clone have the same genetic material and are exact copies of the original.

Complementary DNA (cDNA).- DNA synthesized from a messenger RNA template rather than the usual DNA template. cDNA is often used as a DNA probe to help locate a specific gene in an organism.

Cosmids.- Plasmids into which phage lambda cos sites have been inserted; as a result, the plasmic DNA can be packaged in vitro in the phage coat.

DNA (deoxyribonucleic acid).- The molecule containing hereditary information in all but the most primitive organisms (some viruses that use RNA). The molecule is double-stranded, with an external "backbone" formed by a chain of alternating phosphate and sugar (deoxyribose) units and an internal ladderlike structure formed by nucleotide base-pairs held together by hydrogen bonds. The nucleotide base-pairs consist of the bases adenine (A), cytosine (C), guanine (G), and thymine (T), whose structures are such that A can hydrogen bond only with T, and C only with G. The sequence of each individual strand can be deducted by knowing that of its partner. This complementarity is the key to the information-transmitting capabilities of DNA.

DNA probe.- A molecule (usually a nucleic acid) of known structure and/or function that has been tagged with some tracer substance (a radioactive isotope or specific dye-absorbing compound) that is used to locate and identify a specific gene or region of a chromosome or portion of the genome.

Domain.- A region of the amino acid sequence of a protein that can be equated with a particular function, or a corresponding segment of a gene.

Endonuclease.- An enzyme that cleaves bonds within a DNA or RNA strand.

Enzyme.- A functional protein that catalyzes a chemical reaction. Enzymes control the rate of metabolic processes in an organism.

Expression.- The process by which the blueprint contained in DNA is converted into the structures and biochemical mechanisms present and operating in a cell.

Gene.- The portion of a DNA molecule that constitutes the basic, functional hereditary unit; a sequence of DNA that produces a specific product.

Gene amplification.- Increase, within a cell, of the number of the same gene. Amplification may be spontaneous or induced.

Genetic engineering.- A technique used to modify the genetic information in a living cell, reprogramming it for a desired purpose (such as the production of a substance it would not naturally produce).

Genotype.- The total of the genetic information contained in the chromosomes of an organism; the genetic makeup of an organism.

Hybridization.- In molecular genetics, pairing of an RNA and a DNA strand or of two different DNA strands.

Messenger RNA (mRNA).- An RNA transcribed from the DNA of a gene, forming the template from which a protein is translated.

Molecular genetics.- The study of the nature and biochemistry of the genetic material. Includes the technologies of genetic engineering that involve the direct manipulation of the genetic material itself.

Monoclonal antibodies.- Antibodies derived from a single source or clone of cells that recognize only one kind of antigen.

Mutation.- Any changes that alters the sequence of bases along the DNA, changing the genetic material.

Nucleic acid.- A polymer composed of DNA or RNA subunits.

Phage.- See Bacteriophage.

Phenotype.- The observable properties of an organism resulting from the interaction between its genotype and the environment.

Plasmid.- Hereditary material that is not part of a chromosome. Plasmids are circular and self-replicating. Because they are generally small and relatively simple, they are used in recombinant DNA experiments as acceptors of foreign DNA.

Promoter.- Sequence of DNA giving the starting signal for transcription.

Protein.- A linear polymer of amino acids; proteins are the products of gene expression and are the functional and structural components of cells.

Recombinant DNA (rDNA).- DNA molecules that have been assembled with the use of restriction enzymes, usually but not always by splicing together fragments from different species.

Replication.- The formation of two new strands of DNA from existing DNA, permitting the reproduction of an identical new cell as the result of the division.

Restriction endonuclease.- See Restriction enzyme.

Restriction enzyme.- A nuclease that recognizes specific sequences in DNA and cleaves the DNA strand at those points; used in recombinant DNA technology.

Ribonucleic acid (RNA).- A polynucleotide consisting of a backbone of alternating phosphate and sugar (ribose) molecules to which are attached the nucleotide bases adenine (A), thymine (T), guanine (G), and uracil (U), which replaces the cytosine (C) of DNA. There are several classes of RNA that serve different purposes, including messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA).

Transcription.- The synthesis of RNA or DNA template.

Transduction.- The process by which foreign DNA becomes incorporated into the genetic complement of the host cell.

Transfection.- The process of forcing cells to take up DNA from the external environment.

Transformation.- The transfer of genetic information by DNA separated from the cell.

Transgenic.- A state whereby an organism contains within its germ-line genome both parental and foreign DNA sequences.

Translation.- The synthesis of a polypeptide with an amino acid sequence derived from the codon sequence of a corresponding messenger RNA.

Translocation.- The transfer of a segment of one chromosome to another chromosome. If two nonhomologous chromosomes exchange pieces, the translocation is reciprocal.

Vector.- A transmission agent; a DNA vector is a self-replicating DNA molecule that transfers a piece of DNA from one host to another.

Virus.- An infectious agent that requires a host cell in order for it to replicate. It is composed of either RNA or DNA wrapped in a protein coat.

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See adjacent page for references and brief summary of prescribing information.

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Indications and Usage: 1. *Active duodenal ulcer*–for up to 8 weeks of treatment. Most patients heal within 4 weeks.

2. *Maintenance therapy*–for healed duodenal ulcer patients at a reduced dosage of 150 mg h.s. The consequences of therapy with Axid for longer than 1 year are not known.

Contraindications: Known hypersensitivity to the drug. Because cross sensitivity in this class of compounds has been observed, H_2-receptor antagonists, including Axid, should not be administered to patients with a history of hypersensitivity to other H_2-receptor antagonists.

Precautions: *General*–1. Symptomatic response to nizatidine therapy does not preclude the presence of gastric malignancy.

2. Dosage should be reduced in patients with moderate to severe renal insufficiency.

3. In patients with normal renal function and uncomplicated hepatic dysfunction, the disposition of nizatidine is similar to that in normal subjects.

Laboratory Tests–False-positive tests for urobilinogen with Multistix® may occur during therapy.

Drug Interactions–No interactions have been observed with theophylline, chlordiazepoxide, lorazepam, lidocaine, phenytoin, and warfarin. Axid does not inhibit the cytochrome P-450 enzyme system; therefore, drug interactions mediated by inhibition of hepatic metabolism are not expected to occur. In patients given very high doses (3,900 mg) of aspirin daily, increased serum salicylate levels were seen when nizatidine, 150 mg b.i.d., was administered concurrently.

Carcinogenesis, Mutagenesis, Impairment of Fertility–A 2-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a 2-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a 2-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny

Pregnancy–Teratogenic Effects–Pregnancy Category C–Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect; but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in 1 fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in 1 fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers–Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use–Safety and effectiveness in children have not been established.

Use in Elderly Patients–Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events were due to the drug.

Hepatic–Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to 3 times the upper limit of normal, however, did not significantly differ from that in placebo patients. All abnormalities were reversible after discontinuation of Axid. Since market introduction, hepatitis and jaundice have been reported. Rare cases of cholestatic or mixed hepatocellular and cholestatic injury with jaundice have been reported with reversal of the abnormalities after discontinuation of Axid.

Cardiovascular–In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in 2 individuals administered Axid and in 3 untreated subjects.

CNS–Rare cases of reversible mental confusion have been reported.

Endocrine–Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic–Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H_2-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported

Integumental–Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported

Hypersensitivity–As with other H_2-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other–Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage. Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis does not substantially increase clearance of nizatidine due to its large volume of distribution.

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50 Years Ago

From the *Journal of the Connecticut State Medical Society*

September 1941

The Line Forms On the Left

On the morning of September 16 Yale University will again open its doors to the members of the Connecticut Clinical Congress. Coming each year just prior to the opening of the University activities this event also marks the beginning of a sort of fiscal year for the Connecticut doctor. Vacation days and summer heat have been dissipated, forgive the word, but the present season is twice blest for the return of the oyster is also accompanied by our finest fall weather. The time has come for the doctor to roll down his sleeves and fold away his white flannels, for now he proposes to think more seriously of his task. So mid September finds him again in New Haven preparing to take a pleasant, if heroic dose of postgraduate medicine. And massive the dose really is, but so adroitly divided and so highly concentrated by the Program Committee that its tonic effects are both immediate and lasting.

The Connecticut Doctor has a right to be proud of his Clinical Congress for its success and reputation have extended far beyond the bounds of his little "land of steady habits." Evidence of this is quite at hand, for other assemblies of a similar nature in various parts of our country have studied carefully this pioneering Connecticut enterprise. A remarkable thing about this yearly "brush-up" is its continued and growing vitality. Each year has seen surprising and ingenious innovations some of which have been frankly experimental, in itself a sign of healthy growth. A survey of this year's program proves no exception. In addition to the more formal part of the program the new Yale Medical Library will welcome our members to view its treasures and become familiar with the many opportunities which have been developed for their service. The opening of this great medical library is truly an event of moment for the physician of Connecticut. However, in addition to our deep gratitude for these privileges comes to each of us also a sincere sense of obligation. We in turn can serve this great library which will serve us, for ours is the opportunity to support its plans for development and to add to its collections.

Elsewhere in this issue appears the complete program of the 1941 Clinical Congress. Study reveals that the Program Committee has carefully chosen for discussion those topics which are of more than ordinary interest. Our sincere congratulations go to this group of our members for their excellent judgment and sincere devotion to an important duty.

Judging from past experience the line forming at the left of the registration desk on the 16th will be a lengthy one. You will save yourself a good deal of time and fumbling by registering right now! Many wise ones have already done so.

—Editorial from *The Connecticut State Medical Journal*, September 1991.

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HELPFUL HINTS

Who is Center on the Team?

E. TREMAIN BRADLEY, M.D.

OUR 3,000 bed army hospital during World War II received trainloads of casualties who had been treated in three to eight installations in the European theater. Sixty of these men were on my two wards, and surgical consultation for the other 2,940 fell to my responsibility. Seldom was there precedent for the multiple and bizarre injuries. What was our objective, the optimum end result we sought for each soldier? What should it be for each of our patients in civilian practice too?

Oh, that's simple: just get the patient well as thoroughly, quickly, comfortably as possible. We run the tests, use our modern diagnostic equipment, then prescribe medication and sometimes perform surgery. We were taught scientific medicine in medical school and should use it. But we need the help of a vital part of the team – the patient.

Most patients today have some knowledge of medicine, right or wrong. It is important to hear their questions and be sensitive to the anxiety or fear that is apt to accompany an illness. Is there a good relationship with the patient: who trusts, whose questions are answered, and who feels that his doctor really cares about him? Not as some say, that they have had a lot of tests and bills and a lot of doctors, but nobody really knew me, or cared. I wonder if this concern – sympatico – would be more prevalent if the medical school faculties included fewer full-time and more members with experience in private practice, where the families, the finances, the emotions are more acutely involved, where appraisal and treatment must especially be practical. The academic teaching, of course, is imperative too, for the rare diseases, the special techniques and instruments.

At the time I retired I was treating individuals in the same family as when I started 37 years earlier. I like to call mine a "family practice of surgery" where I treated *people* who might or might not need surgery, rather than treating disease that happened to be in people. Each one was treated as if a member of my family, with gentleness, dignity, and honesty. True, some were not cured. We tried to make those comfortable, and to help the dying go comfortably and with dignity.

The team approach is important. And in order to do his part the patient must understand what the problem is, what the goal is, what to expect (good or bad), what to avoid, when to ask for help, and when to be independent.

"Do unto others as …." the Golden Rule says. Let's treat the *whole* patient – with LOVE.

E. TREMAIN BRADLEY, M.D., solo practice of general surgery, retired to Norfolk, CT.

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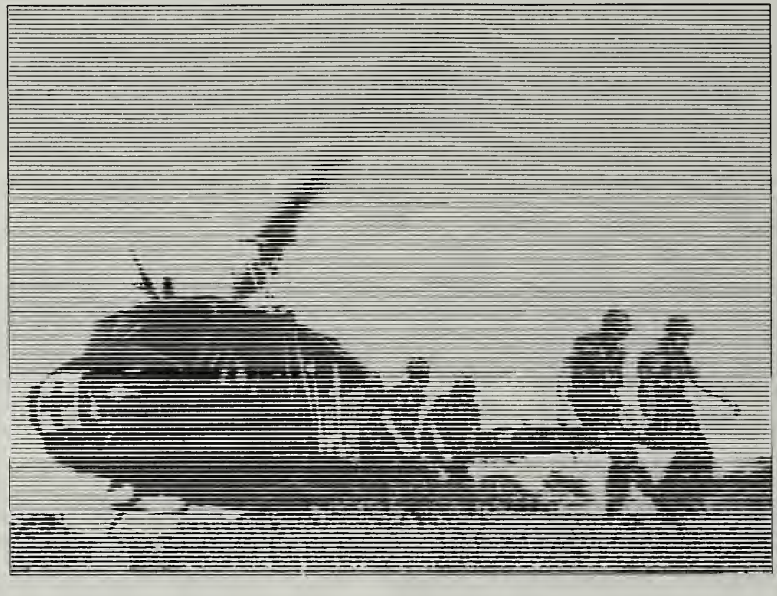

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The Leading Edge?

Medicare was started by an act of Congress in 1965 to provide health care coverage for all those over 65 years old. It is divided into two parts, and applies to those over 65 who are working or who are retired.

The first, Part A, is the hospital insurance. This is available to all who have paid Social Security for a certain number of years and even to those who have not. Those who have not paid Social Security are able to purchase it, and this year, 1991, it costs $177 per month. Hospital insurance covers hospitalization, a small amount of skilled nursing home care, home health care, and hospice care. These costs are mostly covered although there is sometimes a deductible.

The second part, Part B, is the medical insurance to pay doctor bills, etc. Essentially, each year every patient pays the first $100 dollars and 20% of the allowable charges thereafter. Medical insurance is something that the recipients of part A elect to pay. This year part B costs $29.90 a month. If one delays purchasing this medical insurance, the premium increases by 10% for every twelve months one puts off purchasing it. There is open enrollment for medical insurance only in the first three months of each year. There is no means test, and Medicare currently subsidizes health care for over 500,000 millionaires.

Currently the cost of Medicare is approximately 116 billion dollars. One might wonder how many people are actually on Medicare. The figure varies, but it is approximately 33 million people. If one divides the Medicare budget of 116 billion by the 33 million recipients you come up with a figure of $3500. This, the administration would have us believe, is the amount of money spent on each Medicare recipient this year. Where does this money come from? The workers of America supply it. Everybody who works and his/her employer contribute 2.9% of wages up to $125,000. This works out that a person who earns $25,000 a year pays $725 for Medicare, $50,000 pays $1,450, $100,000 pays $2,900, and $125,000 pays $3,625. If the numbers of workers in each category were available, then we could see exactly where the government obtains the majority of the $116 billion needed to finance Medicare.

Now let us take a step back and see how this money is spent. According to the Office of Management and Budget, 7% goes for the administration of the program. The reason that this figure is so low is that the program has shifted many of the administrative expenses to the physicians and the hospitals. Approximately 43% of the Medicare budget goes to physicians, and I would point out that of this 43% that goes to the physicians 47%, according to HCFA, is spent on office overhead. The other 57% goes to other health care providers, namely the hospitals, nurses, physiotherapists, pharmacists, etc. These people also have their own overhead and paperwork costs. (My hospital claims that 37% of every dollar received is spent just on paperwork.)

Medicare is important to those over 65, but it is also the leading edge of a wedge. I can assure you that any change made by Medicare will be monitored by all of the insurance companies and big business when looking to control health care costs in the future.

It would appear at this time that the government feels that the workers have been taxed enough. When Social Security was started by President Roosevelt in the 1930s, there were about 11 workers for every person on Social Security. Now there are fewer than three for every person on Social Security. The fact of the matter is that there is dwindling support in America for health care and many critics think that we are already spending too much of the GNP on health care. How are we going to keep paying for good health care? We certainly have the best in the world.

The role of the government in this is obviously important, but it should not become dominant as it is now in Medicare and in England, because once one has centralized government involvement, the paperwork and expenses increase tremendously, as they have already for Medicare. Once basic access and coverage is assured to all, our private health care system should be protected.

Anthony P. Redmond, M.D.
President

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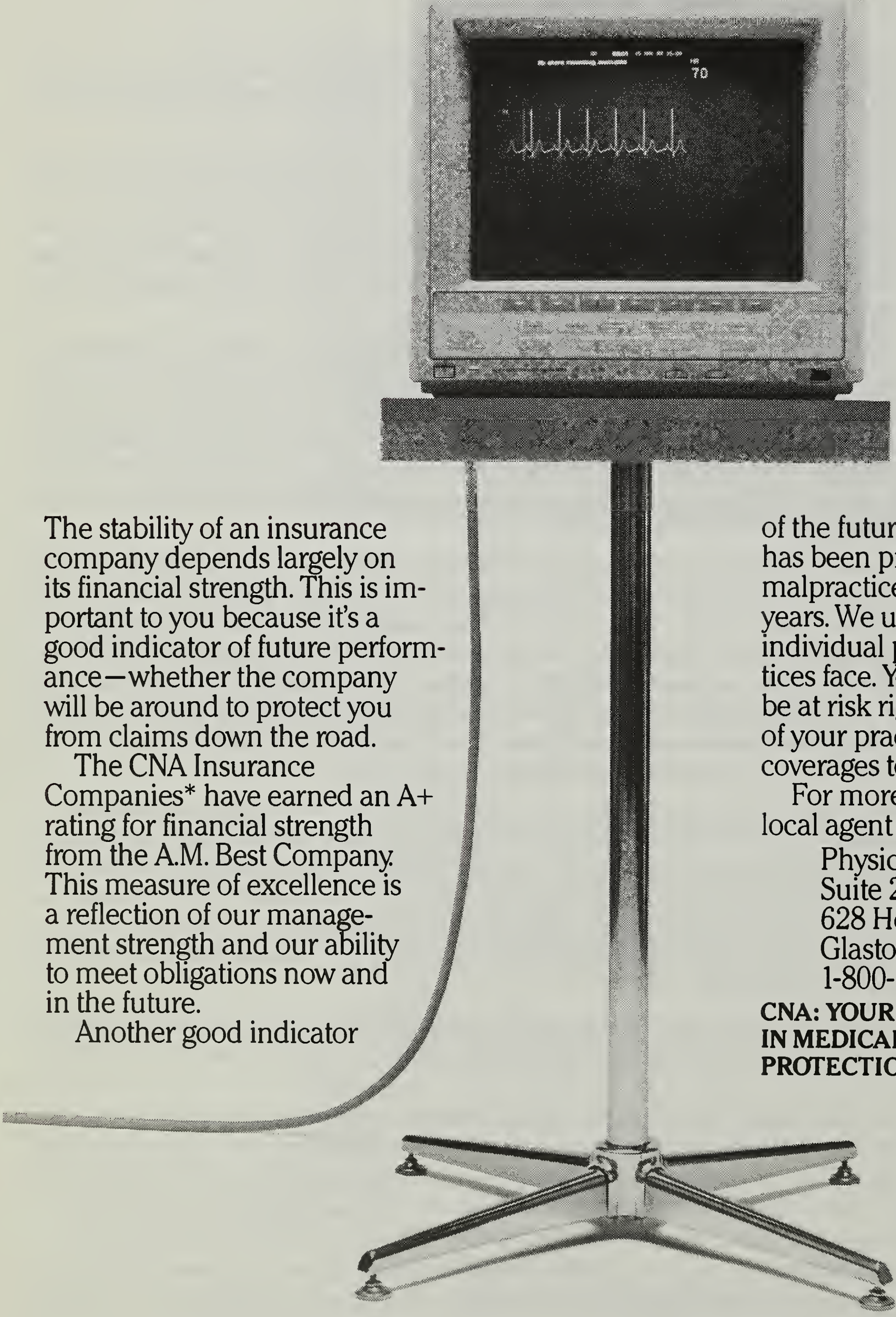

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History's Uncertainty Principle

ROBERT U. MASSEY, M.D.

> For I dipped into the future far, as human
> eye could see.
> Saw the Vision of the world, and all the
> wonder that would be:
>
> ……
>
> Heard the heavens fill with shouting, and
> there rain'd a ghastly dew
> From the nations' airy navies grappling
> in the central blue;
> Till the war-drum throbb'd no longer,
> and the battle-flags were furled
> In the Parliament of man, the Federation of the world.
> —Tennyson, "Locksley Hall," 1842

TENNYSON'S prophetic poem was a favorite of many of us in the late 1930s. Surely the world was getting better in spite of the Great War of 20 years before which Tennyson, we were sure, had foreseen. The superiority of America's democratic order must, in spite of temporary setbacks in Europe, be apparent to everyone. Tennyson saw the future, and so could we; it was not some formless mystery, rather inevitable progress, and quite predictable.

So we believed, but the events of the next half century made us doubt our ability to predict events and to control the course of history by legislation and monetary manipulation. Recently a colleague mentioned an organization called "Physicians for a national health program"; another interjected, "For heaven's sake, I hope they don't propose *doing* anything; no matter what their plan, it can only make matters worse!"

Too often we have seen a scheme for solving some social problem turned into legislative action that made the situation worse. The law of the unintended effect is as evident in political affairs as it is in medicine: increase welfare support and poverty spreads and deepens; increase teachers' salaries and SAT scores fall faster than ever; reduce the incidence of fatal myocardial infarction and increase the numbers of frail and dependent elderly. There is a deeper structure in human affairs that we may know intuitively but rarely understand.

When the reign of communism fell in Eastern Europe, when Germany was reunited, when, after more than 70 years of Marxist rule in the Soviet Union, the system disintegrated before our eyes, we were surprised. In West Germany three years ago I heard seasoned German journalists say that reunification any time soon was highly unlikely. Last month events in Moscow had about them a quality of unreality as though all familiar landmarks had shifted overnight; last year even China experts could not interpret what was happening in Tiananmen Square. In clinical medicine we are less easily surprised; in spite of the splendid work of molecular biologists, their insights have not made us confident that we know how the organism really works. We acknowledge, or should, deeper structures, systems, and purposes that may someday be elucidated, but must for now appear as though "through a glass darkly."

In writing of recent political events in Europe and the Middle East, W. R. Connor asks, "Why were we surprised?" In this world of "radical indeterminacy" he suggests:

> A greater attunement to emotional and moral factors, to the persistent claims of primary attachments, and of religious, ethnic, and national identities must be at the core…, not an afterthought or a concession to the importance of factors that have hitherto been undervalued. We badly need a fresh approach…that is grounded in the serious study of culture and the long-term nature of historical change.[1]

Connor, noting that historical analogies are heuristic, not predictive, urges that we develop a "practical intelligence," a willingness that recognizes that "plans rarely work out as expected and ironic outcomes are to be anticipated." Surely as we work our way through major changes in the provision and financing of health care, we need to heed the lessons of recent history (and ancient as well) that this is a "world of unexpected outcomes."

REFERENCE

1. Connor WB: "Why were we surprised?" *The American Scholar.* Spring 1991; 60:175-84.

ROBERT U. MASSEY, M.D., Professor, Division of Humanistic Studies in Medicine, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

Access to Food Constitutes a Human Right

World hunger is an ever-present scourge that claims 35,000 lives each day. We so frequently take for granted our job opportunities, our very comfortable homes and our ability to feed, clothe and educate our children. While we take for granted all this abundant goodness, three children are dying of starvation or hunger-related diseases every 10 seconds of the day.

Access to food constitutes a human right. In 1976, the United States Congress passed a Right to Food Resolution which declared the sense of the congress to be "that all people have a right to a nutritionally adequate diet". **Physicians Against World Hunger** (PAWH), a non-profit, tax-exempt organization was founded so that physicians could collectively defend this human right by raising funds to support well-recognized, reputable organizations that are directly engaged in working with the poor primarily for the purpose of ending death by starvation.

Please do not ignore this plea. On PAWH day—the third Tuesday in October—please donate your earnings to help end world hunger. It may be the single most important life-saving measure you will take that day. Please don't turn your back on your fellow man whose only fault was to have been born at the wrong time in the wrong place. Together physicians must help bring an end to this genocide.

Physicians Against World Hunger

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Taking Fiduciary Relationships Seriously

JOSEPH M. HEALEY, J.D.

THE *Moore* case, discussed in my most recent columns, has heightened sensitivity about the existence of potential, apparent, or actual conflicts of interest within the doctor-patient relationship. In raising issues about one example of such conflicts, the use of patient information, data, organs, cells, or body parts for research or commercial benefit without the patient's knowledge or consent, the *Moore* case has focussed our attention upon the fiduciary nature of the doctor-patient relationship. There are at least four other examples of conflicts of interest in the doctor-patient relationship: (1) the offer, recommendation, or provision of excessive, insufficient, or inadequate services; (2) direct or indirect financial interest in materials such as drugs or devices that are recommended, prescribed, or sold by the doctor; (3) financial rewards for patient referrals; and (4) the self-referral of patients to facilities or services owned in whole or in part by the doctor. These other examples have also been the subject of increased attention recently. In all five examples, there is an underlying question about the extent to which the doctor is exercising his or her independent judgment for the well-being of the patient. As a participant in a fiduciary relationship, the doctor owes a duty of loyalty to the patient to avoid engaging in conduct that takes advantage of the patient's vulnerability. There are several approaches to managing conflicts of interest. One approach is to prohibit certain conduct on the part of the doctor. A second approach is to impose disclosure requirements designed to assure that the patient has knowledge about the potential or actual conflict. Both the *Moore* case and a recent Connecticut statute employ disclosure of information to the patient as an important strategy to avoid or at least to minimize breach of the fiduciary duty owed by the doctor. Over time, it is likely that such disclosure requirements will assume even greater significance.

In the *Moore* case, the California Supreme Court held that a physician who is seeking a patient's consent for a medical procedure must disclose personal interests unrelated to the patient's health "whether research or economic, that may affect his medical judgment."[1] Such a requirement grows out of the requirement that patients possess sufficient knowledge to exercise an informed choice. This extends the scope of the doctor's duty to disclose beyond discussion of risks and alternatives and into an important, if difficult to define area. At the very least, this requirement will force California physicians to examine the relationship between their personal economic interests and their medical judgments in a more deliberate and systematic manner. It is also possible that this requirement will generate public and professional discussion of just what constitutes an interference with the independent judgment patients expect doctors to employ in pursuing their best interest.

Connecticut physicians will have an initial experience of this process as a result of Public Act 91-168 ("An Act Concerning the Costs of Diagnostic Tests"). Among the requirements of the statute is the disclosure by a health professional of ownership or investment interest in an entity operating diagnostic imaging equipment. The disclosure must be made prior to ordering the test and must also provide reasonable referral alternatives. The requirement does not apply to in-office ancillary services, or the the ownership of investment securities purchased by the practitioner on terms available to the general public and which are publicly traded.

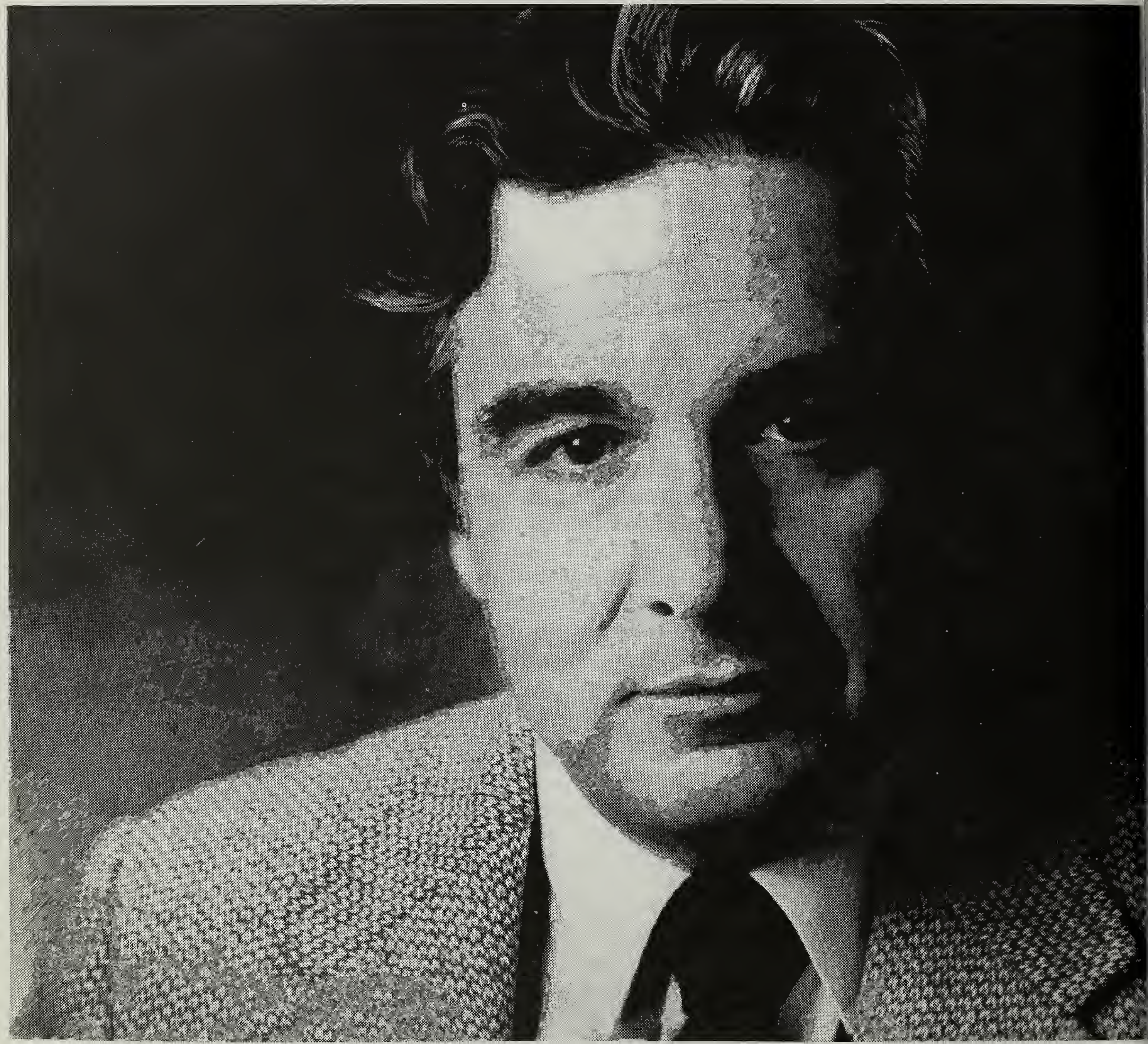
These examples of imposed disclosure requirements reflect a concern that some doctors place their own financial self-interest above the interest of the patient. In promoting disclosure of actual or potential conflicts of interest, the California Supreme Court and the Connecticut legislature have reminded doctors of their obligation to take seriously the nature of fiduciary duties in the doctor-patient relationship. The likelihood is that there will be many more such efforts in the future.

JOSEPH M. HEALEY, J.D., Associate Professor, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

REFERENCE

1. *Moore v. Regents of the University of California*, 793 P2d 479, 485 (Cal, 1990).

"I'm accountable to my patients, not to an insurance company. That's just the way I operate."
—Dr. Vincent Catrini, General Surgery, Middletown, CT



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The Month's Reading in Review

TIMOTHY B. NORBECK

- A consumer alliance survey of 1,330 clinics found that South Korean physicians spend an average of two minutes and 19 seconds with each patient...Each physician treated an average of 155 patients in a six-hour workday...In 22 of the clinics, physicians treated more than 350 - about one per minute...On average, pediatricians saw 223 patients a day, dermatologists 180 and internists 166.
- When asked in a Fortune poll of CEOs, "Of the following factors, which two or three do you consider the most important when it comes to driving up the cost of health insurance for U.S. companies", liability awards and malpractice insurance led the way with 79 percent followed by expensive new technology at 59 percent and unnecessary surgery and other procedures, 52 percent.
- The number of those in the United States over 75, the age at which many people's health begins to deteriorate rapidly, has increased from 5.6 million in 1960 to 13.2 million today.
- Notwithstanding the millions of intelligent, happy, well-cared for children growing up in America, today's generation of young people are the first in the nation's history to be less healthy, less educated and less likely to prosper than their parents...As noted by columnist Paul Taylor, children have been this country's big economic losers of the past two decades...They are nearly twice as likely to be poor as adults - an age bias unknown elsewhere in the world.
- Among 1989 medical school graduates, 81 percent had an average debt of $42,374...Some 29 percent had debts in excess of $50,000...Almost 91 percent of minority graduates were indebted and 41 percent of them had debts above $50,000.
- The Health Insurance Association of America (HIAA) estimates that the number of long-term care insurance policies has doubled from 815,000 at the end of 1987 to more then 1.65 million in June of 1990...Most policies are purchased by individuals but a growing number of companies are sponsoring coverage for their employees...By June of 1990, almost 80,000 people were enrolled in such plans which represents an increase of 60,000 from January, 1989.
- Vice President Dan Quayle's remarks on August 13 to the American Bar Association in Atlanta were coolly received...He said that there were too many lawyers in the U.S., too many lawsuits and too many excessive damage awards...We have 281 lawyers per 100,000 population compared to 82 in England and 11 in Japan.
- By December of this year, Canada hopes to have reduced per capita use of cigarettes by an impressive 25 percent in just three years...Virtually all cigarette advertising has been banned, including even brand names on T-shirts...Health warnings are now required to take up 20 percent of the front and back of all cigarette packs and will be even larger in 1992.
- A Wall Street Journal/NBC News poll conducted in late June indicates that voters are "deeply dissatisfied with the current health-care system and believe that it is up to the federal government to do something about it"...Seven in 10 of those surveyed support requiring everyone to pay some share of their medical expenses as an incentive to use the system less and hold down costs...The poll revealed, however, that many voters seem to draw the line at attempts to ration health care...By 52 percent to 42 percent, they are unwilling to limit the types of tests and procedures available under insurance and government programs...Pollsters Hart and Tester state that when it comes to quality of care, that is one area where "Americans will not compromise to control costs."
- Hershey Foods Corporation will be asking its 650 nonunion workers to report to a company health-screening site later this summer where they will be weighed, measured, and prodded for details about their smoking and exercise habits...It's part of an experimental program designed to cut health-care costs...Under the plan, employees who fall short in five risk categories (tobacco, blood pressure, weight, exercise and cholesterol) - and fail to improve their standing- could lose as much as $1,404 a year in health-care benefits.
- The $23,200 pay raise the U.S. Senate voted itself in late July was full of intrigue...This action required approval by the House of Representatives...Republican and Democratic leaders worked out a plan for a voice vote so that no Members would be on record in favor of the raises...Not going along with the plan, a Congressman from Pennsylvania demanded a recorded vote, an action which required 25 Members to second him...He got only four, so the voice vote prevailed.

TIMOTHY B. NORBECK is Executive Director of the Connecticut State Medical Society.

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Letter to the Editor

Letters to the Editor are considered for publication (subject to editing and abridgment), provided that they are submitted in duplicate, signed by all authors, typewritten in double spacing, and do not exceed 1½ pages of text (excluding references). They should not duplicate similar material being submitted or published elsewhere. Letters referring to a recent Journal article should be received within six weeks of the article's publication.

CONSERVATIVE TREATMENT FOR MYOCARDIAL INFARCTION

To the Editor: Only 70 years ago a surgeon declared that the heart would forever lie beyond the reach of the surgeon. But hypothermia and extracorporeal circulation came out of the laboratory and into the operating room (to aid the anesthetist maintain suspension of function during surgery) and access to the interior of the heart became feasible.

The American problem of myocardial infarction (because of 40% fat in the diet) wedded to American technology soon made cardiac catheterization a popular diagnostic tool. And the venous bypasses that had saved arteriosclerotic lower limbs from amputation began relieving angina the way it had helped claudication.

Therapy of MI has relied heavily on the clinical diagnostic evaluation of chest pain, a subjective sensation. As weighty a surgical decision as coronary bypass, needing solid objective evidence as well as preoperative information, established the need for catheterization labs in metropolitan hospitals. So training for the teams needed for this new diagnostic procedure (with its risk) went bravely forward.

And then it was noted that coronary arterial strictures did not always have pain, so "silent ischemia" was discovered. But little note was made of the personality and situation variations associated with elicited pain. How many clinicians do a Libman test (pressure on the styloid process under the mastoid bone) to determine the patient's pain threshold?

One sturdy, active physician underwent three coronary bypasses before deciding to depend on purely conservative medical therapy. The great challenge and opportunity for surgical intervention in heart disease therapy has been brilliantly met. But pharmacotherapy with calcium channel blockers and beta blockers has also made monumental strides. Is it not time in therapy to make life style modification, and to have a clinical awareness for attuning the cardiovascular demand to the estimated capacity of ejection-fraction capability? Just as exercise programs are prescribed, are there not patterns of respiratory behavior which have myocardial significance?

The Valsalva maneuver deals with arrest during cardiac catherization. Could not self-help muscular contractions and forced respirations restore harmony between supply and demand for blood flow and oxygen level in perceived moments of subjective distress?

Sidney Vernon, M.D.

Willimantic

JOSEPH J. BELLIZZI, 1921 TO 1991

To the Editor: The recent death of Joseph J. Bellizzi, M.D., removed from our midst a truly exemplary pediatrician, the like of which may be passing from the scene. For approximately 40 years he conducted a busy practice in his native Hartford and had attained senior status prior to developing the illness which overtook him two years ago; even then, he did not cease his professional activity, continuing to see patients on a limited basis and to serve as supervising physician for the Hartford school system.

He was a reserved and thoughtful man who could often be found, frequently late in the evening, on the inpatient floor or in the newborn nurseries of St. Francis Hospital, which he loved and served so well, and one can ponder whether such intensity could have led to the illness which ultimately deprived him of the chance to move gradually into the retirement which most of us likely deserve. As an admiring colleague and a father whose children were the beneficiaries of his professional excellence, I stress his constant availability, noting that his home telephone number was always listed in the public directory.

In brief, his performance as a knowledgeable, competent, and sensitive pediatrician can clearly serve as a standard to which many may aspire, but few have equaled. Our sympathy goes to his devoted wife, Lucille, his excellent children, and the grandchildren whom he had barely begun to know. He will truly be missed.

William E. Hart, M.D.

West Hartford

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Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

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References:
1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
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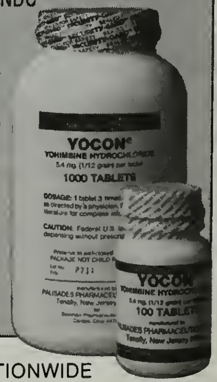
Rev. 1/85



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From the Executive Director's Office

COUNCIL MINUTES

Thursday, August 14, 1991

Attendance

Present in addition to the Chairman, Dr. Joseph C. Czarsty, were Drs. Ahamed, Beck, Blum, Bobruff, Brooks, Deren, M. Fox, Hollister, Keating, McDonnell, Meridy, Parke, Petrie, Redmond, Sosa, Wetstone, Wolfson, Zanker.

Also present: Mr. Norbeck, Mrs. Lindquist, Mr. Brunell, Mr. Garofalo, Dr. Ill, Dr. Van Syckle, Mr. Tomat (FCMA), Mr. Thompson (FCMA), Mr. Freberg (NHCMA), Ms. Shaffman (HCMA)

Absent were: Drs. Blake, Cottle, Dardick, Eslami, B. Fox, Franklin, Freedman, Hosking, Kamens, Lesnik, Orphanos, Parikh, Petro, Sadowski, Van Nostrand, Tesoro, Zeppieri.

Introductions

Mr. Leonard Tomat, retiring Executive Director of the Fairfield County Medical Association, introduced his successor Mr. Mark Thompson.

Dr. Czarsty introduced Dr. David W. Parke, new Associate Councilor from New Haven County Medical Association.

Reports on Related Organizations

M.D. Health Plan: Dr. Guy W. Van Syckle distributed a written progress report on M.D. Health Plan which stated that M.D. Health Plan had completed its 10th consecutive profitable quarter. Enrollment is currently exceeds 57,000 and physician membership stands at 2,937. In spite of the Plan's continued success, the CSMS-IPA's cost has risen dramatically over the past three years, but the Plan's reserves still remain well in excess of the State's mandated levels. Dr. Van Syckle discussed the following issues: the M.D. Health Plan subscribers now having open access to allied health professionals which could increase utilization costs, the withhold return, utilization review policy, etc. He stated that despite rumors which began when MDHP opened its doors that it would be bankrupt, there is no evidence giving credence to those rumors.

CMIC: Dr. Sultan Ahamed reported that at the last Board meeting, the subject of service agreements held with the county associations for service provided by them was discussed. It was suggested that since CSMS is very active in marketing the plan, that some kind of relationship with CMIC should exist and one of the items passed by the Board was to create a service contract between CMIC and CSMS. It was VOTED that the Council approve the development and implementation of a service contract between CSMS and CMIC.

Physician Contracts with Blue Cross/Blue Shield: Having been asked by the Council to bring the subject of Blue Cross/ Blue Shield's termination of physician contracts to the Medical Advisory Committee of BC/BS, Dr. Neil Brooks reported that it was the conclusion of the Medical Advisory Committee that this did not fall under its charge. It is BC/BS's contention that the contract exists between BC/BS and the physician, and that the contract clearly states that it may be terminated by either party without cause. This contractual language allows these contracts to be terminated without having to make statements which may be adverse to the physician's interests. It was VOTED to accept the report for information.

Report of the President

Dr. Redmond discussed Public Act 90-134 which was enacted last year as the result of the Blue Ribbon Commission. This Act mandates the development of a health insurance policy that had to be offered by all insurance companies including Blue Cross and Blue Shield. He noted that small groups of less than twenty-five can be one or two people. However, these groups are rated according to the health of the group, which means employers may be asking health questions of prospective employees. This insurance is expensive and really doesn't answer the problem of the uninsured.

He reported that physicians in Fairfield and Hartford County this fall, and in the other counties at a later date, will be offered an HIV income protection policy by Lloyds through the Watson Agency. The AMA is also offering HIV insurance on a trial basis in eight states, not yet in Connecticut.

He stated that he was invited to address the annual meeting of AARP in September and plans to discuss the Medicare issues.

He further reported that following the last House of Delegates meeting, he received a number of letters concerning the meeting and the possibility of having only one House of Delegates meeting, and he noted that in forty of the states, only one meeting is held. He stated that this would be a good topic for the delegates to discuss, since it would be up to them to make this decision. He proposed to bring a bylaw proposal to the Council on this issue prior to the next House of Delegates meeting.

Report of the Executive Director

RBRVS: Mr. Norbeck reported that CSMS was very successful in getting the membership to send letters to their congressional representatives and HCFA concerning the proposed 16% reduction in the conversion factor. Members of the House Ways and Means, Energy, and Commerce Committees and of the Senate Finance Committee have signed letters that the Bush Administration has undermined a commitment Congress made to medical groups in 1989. He stated that word from Washington indicates that a good guess at this time might be that HCFA will adopt a compromise position and reduce the conversion factor to 6% rather than 16%. If so, AMA most likely will not be satisfied and will pursue the legislative alternative, HR 3070, introduced by Pete Stark, which would legislatively prohibit the 16% reduction.

HIV: It was reported that Senator Jesse Helms introduced a bill which passed 81-18 in the Senate pertaining to HIV infected health care workers. It also provided for a $10,000 fine or prison sentence for those who violate the law. Senator Helms has introduced a companion amendment which would permit licensed health care professionals to require an HIV test prior to or while conducting "an exposure prone invasive procedure" (not in emergency situations). If states fail to cooperate they could have their public funds withdrawn. The amendment passed 86-13.

Vice President Quayle: Mr. Norbeck commented on the address of the Vice President at the American Bar Association meeting in Atlanta and the AMA House of Delegates meeting in Chicago. Basically his remarks were that there were too many lawyers in the U.S., too many lawsuits and too many excessive damage awards. A copy of the Vice-President's remarks at the AMA meeting were distributed to members of the Council.

Uninsured: He reported that House Ways and Means Chairman, Dan Rostenkowski introduced a bill relative to expanding health insurance benefits to the uninsured, somewhat like other measures which would require employers to pay a tax or provide coverage for workers—the difference from others is that he would help employers by lowering the age for Medicare eligibility from 65 to 60.

Report of the AMA Delegation

A summary of the 1991 AMA Annual Meeting of the House of Delegates held in Chicago June 23-27 was distributed to all members of the Council with the agenda. Dr. Stewart Petrie, Chairman of the Delegation, highlighted the issues of RBRVS, HIV testing, Bush Administration Professional Liability Proposal and the National Practitioner Data Bank. He reported that the delegates were kept busy at these meetings with the many reference committees and issues that are covered. Dr. Jerome Freedman introduced a resolution concerning third party payors which was accepted for study by the Board of Trustees.

Report on AMA Hospital Medical Staff Section Meeting

Dr. M. David Deren submitted a written report on the AMA-Hospital Medical Staff Section which was held during the AMA Annual Meeting. It was noted that physician payment reform was the number one topic, the Resource-Based Relative Value System (RBRVS). Other issues reported on were HIV infection, concerns about the National Practitioner Data Bank which seems almost unworkable, hospital employment of physicians, practice parameters, managed care and other topics. It was VOTED to accept the report with commendation.

Membership Promotion

At the last meeting staff was requested to prepare ways and means to encourage residents and students to become members of the AMA. Robert Brunell reported that he had been in touch with the AMA to obtain promotional material and as in the past would write a covering letter, over the signature of the student and resident presidents, which has proven to be very successful in obtaining members.

Life Members

It was VOTED to receive the name of the following physicians who were granted Life Membership as of January 1, 1991:

Donn C. Barton, M.D., Glastonbury (M)
A.J. Cappelletti, M.D., Waterbury (NH)
John D. Clark, M.D., Madison (NH)
James A. Harkins, M.D., Niantic (NL)
Carlos Peralta, M.D., Easton (F)
Clement J. Philbrick, M.D., Milford (NH)
Joe W. Trent, M.D., Stamford (F)

Minutes of Ad Hoc Committee on HIV Testing

The minutes included a discussion of HIV Exposure-Prone Procedures, Exposure-Prone Health Care Workers, Occupational HIV- Infection and Disability and the AMA Substitute Resolution 240. Following discussion, the following actions were taken:

(a) VOTED that the Council approve the statement of HIV-Exposure Prone Procedures as outlined, e.g. that all procedures have risk of patient contamination if any blood is exchanged, directly or via instrumentation.

(b) VOTED that the Council approve the statement of HIV Exposure-Prone Health Care Workers as outlined, e.g. those at elevated risk of occupational infection.

(c) VOTED to table the motion that the Council adopt the statement that Occupational HIV-Infection is a disability with respect to insurance coverage for reconsideration and to include more specifics in the wording in their report supporting this motion. It was noted that the last sentence in the first paragraph in the section entitled "Occupational HIV-Infection and Disability" was vague.

(d) VOTED that the Council support the AMA Substitute Resolution 240 on HIV testing of health care workers and patients.

Dates for Future Council Meetings

Thursday, September 19, 1991
Wednesday, October 23, 1991

N.B.: *The foregoing is a summary of the proceedings and actions of the Council on August 14, 1991. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested members of the Society.*

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***Physicians wishing to locate* in Connecticut may call the office requesting opportunities in their specialty. Also, candidates are invited to submit a resume to be kept on file with the Society. An announcement of a physician's availability will be published in two issues of *Connecticut Medicine* as space permits.**

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Jul. '91 M.D., Int. & Res. Univ. of Medicine & Dentistry of New Jersey. Fellowship at Univ. of Medicine-Dentistry of New Jersey and Baylor College of Medicine, TX. Specialty Int. Med./Critical Care/ Pulmonary Care. Prefers opportunity in vicinity of Madison, CT. Write Anjana Shah, 404 S. Fryer's Creek, #114, Temple, TX 76504.

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Hypersensitivity Pneumonitis Associated with a Portable Home Humidifier

BRETT T. VOLPE, M.D., STEPHEN B. SULAVIK, M.D.,
PHUONG TRAN, M.D., AND ANDREA APTER, M.D.

ABSTRACT—Hypersensitivity pneumonitis (HP) is an immunologically mediated inflammatory disorder of the pulmonary parenchyma which has been traditionally associated with the inhalation of organic dusts (farmer's lung, pigeon breeder's disease) and a variety of simple chemical compounds.[1] More recently, the disease has been reported in association with the inhalation of aerosolized droplets in home and office settings.[2-5] In Connecticut, the home and office, rather than the farm or factory, are the most common, although frequently unrecognized, environmental settings in which HP develops. We report here a case of a young, healthy woman who developed severe HP associated with the use of a portable home ultrasonic humidifier. This clinical entity should be suspected in the patient with a "recurrent viral illness" or "recurrent pneumonia." A review of the clinical and laboratory findings of humidifier-induced HP are discussed in relation to its pathogenesis, diagnosis, and treatment.

Case Report

THE patient is a 29-year-old woman who was well until the last week of December 1990 when she awoke at home with frontal headache, nasal congestion, and a temperature of 38.5°C. She saw her physician on the next day and he prescribed cefuroxime 250 mg p.o. b.i.d. for two weeks for acute sinusitis. She noted improvement in symptoms over the next week, but then developed chills and fever with a temperature of 39°C. These symptoms lasted for 12 hours and subsided spontaneously. Over the next two days, she developed dyspnea with walking more than 20 feet and a persistent, dry cough. She returned to her physician and a chest film was taken and reported as normal. Her white blood cell count was 19,400. The physician made the presumptive diagnosis of acute bronchitis and changed the patient's antibiotic to oral amoxicillin/clavulanate 250 mg t.i.d. Despite this regimen over the next two days, the patient noted increasing dyspnea on exertion, cough, malaise, and low-grade temperatures of 38-38.5°C. Her physician advised her to go to the emergency room.

In the emergency room, the patient was afebrile, in no respiratory distress at rest, and her physical examination was normal. A white-cell count of 23,400 with a normal differential and an ambient air arterial blood gas of pH 7.43/PaCO$_2$, 31/PaO$_2$, 83/HCO$_3$, 21 were noted. Her chest film showed increased bibasilar markings. The patient was admitted and treated for a presumed atypical pneumonia with tetracycline. Her temperature was 38°C on the next day, but cough and dyspnea continually improved over the next three days. By 10 January, three days later, the patient felt better and was discharged on oral tetracycline. Ambient air arterial blood gas prior to discharge was pH 7.53/PaCO$_2$, 26/HCO$_3$, 102.

Approximately 16 hours after discharge, the patient awoke with profound dyspnea, dry cough, and a feverish feeling. She returned to the emergency room and was noted to be cyanotic and in moderate respiratory distress with a respiratory rate of 32. Chest examination revealed bibasilar inspiratory rales. Ambient air arterial blood gas was pH 7.35/PaCO$_2$, 40/PaO$_2$, 43/HCO$_3$, 26; her white-cell count was 20,400 with a normal differential. Repeat arterial blood gas on 100% nonrebreather mask was pH 7.35/PaCO$_2$,45/PaO$_2$,219/HCO$_3$,25.The chest film showed no definitive infiltrates. The patient was readmitted and given supplemental O$_2$, pulse oxymetry monitor, and IV tetracycline and trimethoprim/sulfamethoxazole. The patient developed a temperature of 39° several hours after admission but this did not persist. The next day the patient's dyspnea was markedly reduced and her respira-

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BRETT T. VOLPE, M.D., Pulmonary-Critical Care Fellow, University of Connecticut School of Medicine. STEPHEN B. SULAVIK, M.D., Professor and Head, Division of Pulmonary Medicine, University of Connecticut School of Medicine. PHUONG TRAN, M.D., Resident, Internal Medicine, University of Connecticut School of Medicine. ANDREA APTER, M.D., Allergy and Clinical Immunology, University of Connecticut School of Medicine.

tory rate was 20. Arterial blood gas on 1 liter/min O_2 was pH 7.42/PaCO_2, 37/PaO_2, 84/HCO_3, 24. At this time, the patient was questioned about the use of a humidifier at home. She affirmed the continuous use of an ultransonic cold-air humidifier in her bedroom since the initial visit with the internist. The internist had advised her to use the humidifier during sleep in an effort to help treat her sinusitis. The humidifier had been purchased one year prior to this time and was last used in January 1990 for a two-week period. The unit was cleaned thoroughly with dishwashing detergent after this period and not used again until the present illness. As a result of this new information, antibiotics were stopped on 11 January. The humidifier was removed from the patient's home. Humidifier water samples and a sample of the patient's serum were sent to the Connecticut State Laboratory and the Northwestern University Medical School Allergy-Immunology Laboratory. The patient's symptoms resolved over the next two days, and pulmonary function tests performed prior to discharge on 14 January revealed a mild reduction in FEF25-75 which improved significantly with bronchodilator and mild reductions in both lung volumes and diffusing capacity. Ambient air arterial blood gas was pH 7.43/PaCO_2, 38/PO_2, 106/HCO_3, 25.

The patient returned home and experienced no recurrence of symptoms during a two-month follow-up period. The humidifier water fungal cultures grew a *Rhodotorula* species and a *Candida* species. Precipitating antibody testing by gel diffusion technique of an antigen panel to concentrated humidifier water and patient serum revealed a positive precipitin reaction to the *Aureobasidium pullulans* fungal species.

Discussion

Portable ultrasonic humidifiers have been commonly used in homes and offices for the past three decades. Water droplets produced by these devices range in size from 0.5 to 3.0 microns[6] and are therefore small enough to reach distal airway spaces. If the humidifier is not cleaned thoroughly and frequently, the potential for fungal or bacterial water contamination exists. These contaminated water droplets, if repeatedly inhaled, can serve as an antigenic nidus for localized hypersensitivity reaction within the lung parenchyma of some individuals. Although the humidifier reservoir tank can be easily cleaned, there are several relatively inaccessible components such as the aerosol dispersion nozzle and ultrasonic generator that can be potential sources of aerosol contamination.[5]

A variety of microorganisms have been implicated in the development of HP from contaminated ventilation and humidification systems.[3,4,7] Thermophilic actinomycetes, the most notorious of these microorganisms, is rarely cultured from the ultrasonic humidifiers because of the absence of a heated environment needed for the thermophilic species growth. Microbiological and immunological studies of humidifier lung cases report increased prevalence of unusual fungi such as *Sphaeropsidales*[3] and *Rhodotorula*.[8] *Legionella pneumophilia* and *Enterobacter cloacae*[3] are bacteria that have been implicated in this setting as well.

The pathophysiologic consequences of humidifier lung are the same as those that occur with other forms of HP. The immunopathogenesis of HP is not fully understood. There is evidence that both type III (antigen-antibody complex mediated) and type IV (T cell mediated or delayed hypersensitivity) immune mechanisms are involved. Dose of inhaled antigen and T cell/macrophage interaction appear to be key influential factors in the pathogenesis.[9,10] The explanation for why some persons remain unaffected, even when exposed to the same antigenic source that induces hypersensitivity in other persons, is unknown.

The observed pathologic changes of HP are a function of the duration of the hypersensitivity process following the initial antigenic exposure. In the acute and subacute stages (less than three to six weeks following initial antigenic exposure), an interstitial infiltrate consisting of lymphocytes, plasma cells, epithelioid cells, granulomas, and intra-alveolar debris is seen on lung biopsy. Bronchiolitis obliterans has been reported as well.[1] In the chronic stage (greater than six weeks of repeated antigenic exposure), interstitial fibrosis becomes more prevalent so that early clinical recognition of the disease is important.

The early signs of acute HP, which can occur within hours to days following antigen inhalation, are fever, myalgias, malaise, anorexia, and even sore throat and headache. Respiratory symptoms may or may not be initially present. When respiratory problems do develop, they can progress rapidly from mild cough to severe dyspnea and hypoxemic respiratory failure in less than a day. The patient who appears to have a recurrent viral or influenza-like illness or recurrent pneumonia should alert the clinician to the possibility of HP. If the patient has no history of organic dust, mold, or chemical exposures that could implicate a hypersensitivity process, the physician should focus his questioning on the presence of forced-air ventilation systems and portable humidifiers in the home and workplace. A common scenario, as was observed in our case, is the patient who improves within one to two days in the hospital while on antibiotic therapy for a presumed atypical pneumonia, only to return to the hospital within hours to days after rechallenge with the aerosolized antigen in the home or workplace.

With the exception of fever, signs of respiratory distress, and occasionally rales, physical examination findings are frequently not contributory to an appropriate history. Cyanosis occurs in severe hypoxemic cases. Routine laboratory findings often include a leukocytosis which can reach 20-30,000. The absence of hypereosinophilia is an important finding since this helps delineate HP from other pulmonary allergic diseases such as eosinophilic pneumonia and allergic bronchopulmonary aspergillosis. Arterial blood gasses can range from normal or mild respiratory alkalosis to severe hypoxemia (PaO_2 < 40-50 mm Hg) with an enlarged alveolar-arterial gradient. In the acute and subacute stages of disease, chest films may be normal or show patchy infiltrates or a diffuse lesion. Severe hypoxemic respiratory failure can be present even with a normal chest roentgenogram, as was noted with our patient.

If humidifier-induced HP is the presumptive clinical diagnosis, then humidifier parts and water can be both cultured and precipitin tested against patient sera and a panel of appropriate fungal and bacterial antigens. Most state-of-the-art allergy-immunology laboratories do precipitin testing for hypersensitivity diseases using a gel diffusion technique.[11] This involves placing both patient serum and concentrated humidifier water samples in wells onto an agar plate with other antigen-containing wells and observing for precipitating bands which represent antigen-antibody complexes. Since both positive culture and precipitin reaction can occur in an unaffected host and negative results can occur in the patient with HP, these tests are supportive but not diagnostic of HP. Antigen skin testing has no practical role because of high false positive and false negative rates. Inhalation challenge with purified antigen has been shown to reproduce HP signs and symptoms.[3,12] Although this diagnostic maneuver can help demonstrate causality, it is not commonly used in clinical practice. Pulmonary function testing may also serve as supportive evidence for diagnosis, but does not substitute for a good history. Restrictive lung volumes and reduced diffusing capacity are often demonstrated.[13]

If the diagnosis of HP is unclear by history and other clinical data, transbronchial biopsy demonstrating the pathologic findings previously described can be helpful. Broncho-alveolar lavage typically will show a predominance of suppressor T cells. The patient with chronic HP will present with clinical features of interstitial fibrosis such as an insidious progression of dyspnea, diffuse lung lesion with honeycombing in the end-stage process, impairment of gas exchange, and a restrictive ventilatory defect.

The most important intervention to arrest or retard the disease process is to remove the suspected harmful inhalation agent from the patient's environment. In the acute and subacute settings, the majority of patients can expect total resolution of symptoms and a return to normal pulmonary function in days to weeks after the inhalation exposure is stopped. If the disease persists after the patient is removed from the exposure, or if removal of exposure is not feasible, then corticosteroid therapy is indicated and can be effective in arresting the disease process. The patient with chronic HP will have a variable recovery of pulmonary function and respiratory symptoms depending on the extent of interstitial fibrosis that has developed at the time the hypersensitivity process is interrupted.

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Diagnostic Nasal Endoscopy and Functional Endoscopic Sinus Surgery: An Update and Review of Complications

STEVEN B. LEVINE, M.D., ALAN J. GILL, M.D., STEPHEN R. LEVINSON, M.D.,
AND TOM K. COFFEY, M.D.

ABSTRACT—Diagnostic nasal endoscopy and functional endoscopic sinus surgery are relatively new techniques that have expanded our understanding of sinus physiology and the etiologies of sinus pathology. Diagnosis at an early stage of chronic sinus disease demonstrates that pathological changes are often limited to the osteomeatal complex and the anterior sinus group. Early disease refractory to aggressive medical management usually responds to surgical treatment. Surgery in this setting is most often performed under local anesthesia, without nasal packing, with an immediate improvement in the patient's symptoms, and with minimal risk of complications.

Introduction

DIAGNOSTIC nasal endoscopy and functional endoscopic sinus surgery (FESS) are new tools in otolaryngology that are fast becoming popular among physicians and patients. These procedures are transforming the otolaryngologists' approach to the nose and sinuses much the way arthroscopy transformed orthopedic surgery 15 years ago.

Diagnostic nasal endoscopy is a technique performed using fiber-optic telescopes, with magnification, to view transnasal anatomy and to assess the etiology of persistent or recurrent sinus pathology. Aggressive medical management is still the primary treatment modality. Patients who do not respond to medical management are evaluated with computed tomography of the sinuses. Radiographic confirmation may then lead to a recommendation for surgery.

FESS is a technique designed to remove only the diseased tissue without affecting the surrounding normal anatomy. The goal is minimal postoperative discomfort, a lack of external incisions, the omission of uncomfortable nasal packing, and an immediate improvement in the patient's symptoms with resolution of the pathology.

Telescopic examination of the nose and paranasal sinuses had been performed as early as 1901.[1] Messerklinger perfected the technique and described endoscopic anatomy as well as normal mucociliary clearance of the paranasal sinuses.[2,3] In 1985 Kennedy introduced the technique in the United States[4,5] while Stammberger popularized it in Europe.[6,7] In the last six years, it has been refined and described in numerous articles and texts.

Anatomy

There are five distinct paranasal sinuses on each side of the head. Embryologically and anatomically these are divided into the anterior group and posterior group. The anterior group, which consists of the maxillary sinus, anterior ethmoid sinus, and the frontal sinus, drain into the middle meatus, ie, that area which is lateral to the middle turbinate. The posterior ethmoid sinus drains through multiple openings into the superior meatus, and the sphenoid sinus drains directly into the nose through its own opening.

Within each sinus, ciliated respiratory epithelium rhythmically beat and direct mucus towards the ostium. Obstruction of the ostium impedes mucociliary clearance and leads to infection.

Most sinus disease is seen in the anterior group, ie, maxillary, anterior ethmoid, and/or frontal sinuses. The confluence of the ostia of the sinuses in the middle meatus is referred to as the osteomeatal complex. The cornerstone of FESS is directed at relieving obstruction at this level, thereby reestablishing normal mucociliary function and returning the sinuses to their normal healthy state.

Diagnostic Nasal Endoscopy

The traditional anterior nasal examination allows one an overview of the relationship between the nasal septum and the nasal turbinates. Examination with the nasal endoscope assesses the patency of the osteomeatal complex seeking out pathology that cannot be seen by the anterior nasal examination. It is an office procedure performed with a thin telescope and is indicated in patients who have persistent or recurrent sinus symptoms that have not responded to conservative management. Diagnostic nasal endoscopy is performed using topical anesthesia.

Axial and coronal computed tomography of the paranasal sinuses with magnification complements the endoscopic examination. Evaluation of radiographs must be a collaborative effort by the radiologist and the otolaryngologist to reach a proper diagnosis. A full clinical history and report of the endoscopic examination will improve the radiologist's interpretation of the study.

Patients with clinical symptoms of sinus disease, but without radiographic evidence of sinusitis, often have radiographic and endoscopic obstruction of the osteomeatal complex. Obstruction may be due to an architectural anatomic variant or due to mucosal disease. Typical anatomic variants include the development of a sinus air cell within the middle turbinate, ie, concha bullosa, a deviated septum that impacts the middle turbinate and shifts it laterally to obstruct the complex, or curling of the edge of the middle turbinate in a paradoxical manner thereby causing obstruction. These anatomic variants are seen in patients whose sinus symptoms and headaches wax and wane, and are exacerbated by nasal congestion. Mucosal disease is more often associated with constant sinus symptoms. Diffuse mucosal disease requires a search for systemic etiology.

Functional Endoscopic Sinus Surgery

FESS is performed utilizing both the nasal endoscopes and direct vision to identify the anatomic landmarks of the osteomeatal complex. Once the complex has been identified and the anterior ethmoid sinus disease has been resected, the next set of landmarks are used to open the posterior ethmoid sinus, sphenoid sinus, frontal sinus recess, and the natural ostium of the maxillary sinus. The maxillary sinus may also be visualized through a trocar that punctures through the anterior wall via the gingivobuccal sulcus.

In our experience, this surgery may be performed in an outpatient setting. If surgery is limited to the anterior group of sinuses, it is often performed with little blood loss and under local anesthesia with intravenous sedation. Frequently, no nasal packing is necessary and the patient will have an immediate improvement of the nasal airway before leaving the operating room table. Resection of more extensive disease may involve general anesthesia, may result in greater blood loss, and may require a light sponge pack in the sinus cavity for 24 hours.

Postoperative care includes mild analgesics for several days followed by several weeks of intermittent nasal irrigation with saline. This is easily performed at home by the patient, and may be accompanied by the use of nasal steroid sprays. The patient is seen in the office for routine cleaning of the sinus cavity until it is well-healed.

FESS is a modern technique that requires special training to be learned. As with mastoid surgery, it requires an understanding of anatomic landmarks at each layer as landmarks are destroyed or removed and new ones encountered. Cadaver dissection must be an integral part of the training experience.

Traditional Sinus Surgery

Traditional sinus surgery is still the time-proven gold standard for the eradication of sinus disease. It includes the Caldwell-Luc procedure with or without transantral ethmoidectomy, external ethmoidectomy, and frontal sinus obliteration. These techniques are performed through external incisions, have greater associated postoperative morbidity and discomfort, require nasal packing, and necessitate hospital admission. Intranasal ethmoidectomy does not require an external incision, but is greatly facilitated by utilizing the endoscopic approach. Since we have been performing FESS, these procedures have been utilized less frequently but nevertheless remain in our armamentarium.

Complications

Potential complications of untreated sinus disease may include direct extension into the orbit, cavernous sinus, or anterior cranial fossa with meningitis or death. Fortunately these complications are rare. The complications of sinus surgery include intraorbital hemorrhage and blindness. The intracranial complications are mostly limited to cerebrospinal fluid rhinorrhea, but also potential intracranial hemorrhage and death. These major complications must be made clear to all patients before surgery. Minor complications include postoperative facial swelling, periorbital ecchymosis, persistent infection, and excessive bleeding.

The reported incidence of major complications from FESS varies from 10% to less than 1%, and minor complications from 21% to 4%.[8,9,10] These studies include the total number of cases performed and do not subdivide them by pathology and the anatomic sinus group involved.

One hundred consecutive functional endoscopic surgical procedures performed by three of the authors (SBL, AJG, and SRL) were reviewed. There was one major complication and four minor complications. The major complication was a case of intraoperative cerebrospinal fluid rhinorrhea that was repaired endoscopically at the time of the initial procedure, and followed an uneventful course without sequelae. The minor complications consisted of facial swelling, persistent infection, and excessive bleeding. There were no cases of periorbital ecchymosis in our series, and all minor complications resolved without sequelae. All five patients with complications had improvement or complete resolution of their sinus symptoms. In our experience, surgery limited to the anterior group of sinuses resulted in no complications.

Surgery involving the posterior ethmoid sinus or the sphenoid sinus had the greatest risk of complications.

Conclusions

Diagnosis of sinus disease is greatly facilitated by endoscopic examination. Most patients with early disease are cured with medical therapy. Disease refractory to medical management is treated with surgery. FESS often may be performed under local anesthesia and without the use of nasal packing, especially if disease is limited to the anterior sinus group. Surgery in these patients has a minimal risk of complications. The end result of FESS is usually a rapid improvement in the patient's symptoms.

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Intraoperative Transesophageal Echocardiography-An Indispensable Tool in Valve Reconstruction and Congenital Anomalies

SURENDRA K. CHAWLA, M.D. AND JOSE MISSRI, M.D.

SUMMARY

TRANSESOPHAGEAL echocardiography (TEE) with color flow mapping has become an excellent tool for evaluating valve reconstruction and correction of congenital anomalies intraoperatively.

From February 1990 to September 1990 we have utilized TEE intraoperatively in 14 consecutive patients. Their ages ranged from 25 to 77 years, with a mean age of 58.7 years. There were eight males and six females. Twenty-one pathological entities were identified intraoperatively: mitral regurgitation due to posterior leaflet pathology in four; anterior leaflet pathology in four; annular dilatation in two; left to right shunt at the atrial level in five (two with partial anomalous pulmonary venous drainage); aortic regurgitation in two; and one patient each with ostium primum septal defect, Ebstein's anomaly, hypertrophic obstructive cardiomyopathy (HOC), and aortic stenosis.

Based on intraoperative TEE findings, corrective procedures included quadrangle resection posterior leaflet with Carpentier ring in four, chordal shortening and chordal transfer anterior leaflet in four, flexible Duran ring for annular dilatation in two, closure of all atrial septal defects (ASD) with pericardial patch in secundum and sinus venosis type (ligation of small anomalous vein in one), and Dacron patch in primum type, myomectomy for HOC and reconstruction of the tricuspid annulus with Duran ring in Ebstein's anomaly. Two patients with associated coronary artery disease had coronary bypass grafting done.

Following mitral valve repair TEE demonstrated trivial to no mitral regurgitation in eight (seven with repair) and mild regurgitation in one patient. All patients with closure of the ASD had an intact septum. The gradient in HOC was reduced significantly and there was satisfactory anatomical reattachment of the tricuspid annulus in Ebstein's anomaly. TEE prevented replacement or repair in one patient with mitral regurgitation (normal valve morphology by TEE) secondary to severe aortic stenosis.

In conclusion, TEE permits a complete assessment of the mitral and tricuspid valve apparatus, atrial septum, aortic valve, and subaortic area. Intraoperative TEE is an indispensable tool in valve reconstruction and various congenital anomalies in the adult population.

Introduction

The development and use of transesophageal echocardiography (TEE) has been a major advance in the diagnostic imaging of the cardiovascular system. This technique is being applied with increasing frequency because of its advantages over standard transthoracic echocardiography in detecting vegetations due to endocarditis, left atrial thrombi, prosthetic valve dysfunction, aortic dissection, evaluation of valve morphology and severity of regurgitation, and congenital anomalies. Intraoperative TEE provides the surgeon with valuable data as to the need for valve repair and also with data regarding the valve morphology and the mechanism for regurgitation needed to plan optimally the type of repair needed.

Since its availability at our institution, we have utilized this modality intraoperatively in all valve reconstruction procedures and congenital anomalies in the adult population. In this study we discuss our experience utilizing intraoperative TEE in determining the adequacy of surgical valve repair, correction of congenital defects, and myomectomy in hypertrophic obstructive cardiomyopathy..

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Materials and Methods

Patient Population: From February 1990 to September 1990 we have utilized TEE intraoperatively in 14 consecutive patients with a diagnosis of mitral regurgitation, mitral stenosis and regurgitation, tricuspid regurgitation due to Ebstein's anomaly, hypertrophic obstructive cardiomyopathy, and atrial septal defect primum and secundum type (Table 1). All patients had right and left heart cardiac catheterization and coronary angiography.

These patients ranged in age from 25 to 77 years, with a mean age of 58.7 years. There were eight males and six females. Nine patients were diagnosed to have mitral regurgitation, six patients had left to right shunt at the atrial level, and one patient had combined pathology.

Among the nine patients with mitral regurgitation, pure mitral regurgitation was diagnosed in three patients, mitral regurgitation and coronary artery disease in two patients, mitral regurgitation and aortic regurgitation in two patients, and aortic stenosis and atrial septal defect in the remaining two patients.

Among the six patients with atrial septal defect, isolated ostium secundum defect was diagnosed in three patients (two with associated partial anomalous venous drainage). Ebstein's anomaly, hypertrophic obstructive cardiomyopathy, and mitral regurgitation were diagnosed in the remaining three patients.

Transesophageal Echocardiography: Following the induction of general anesthesia and endotracheal intubation, TEE was performed using a Hewlett-Packard ultrasound imaging system and a 5 mHz transesophageal transducer. Tomographic imaging planes were obtained as a series of short-axis views (transverse plane) of the heart. Color flow Doppler imaging was obtained to assess the severity of valvular regurgitation and atrial septal defects.

Imaging was performed immediately before and after cardiopulmonary bypass but prior to disconnecting the cannulae. The esophageal probe was left in place during the cardiac surgical procedure. A systolic blood pressure of greater than 100 mm Hg was considered a minimum requirement to assess the adequacy of the repair procedure and to detect associated complications such as outflow tract obstruction.

Table 1

Transesophageal Echocardiography	
Mitral regurgitation (M.R.)—pure	3
M.R. with coronary artery disease	2
M.R. with aortic regurgitation	2
M.R. with aortic stenosis	1
M.R. with atrial septal defect (A.S.D.)	1
A.S.D. —pure	2
A.S.D. with hypertrophic obstructive cardiomyopathy	1
A.S.D. with Ebstein's anomaly	1
Partial anomalous venous drainage	1
Total:	14

Table 2

Transesophageal Echocardiography Intraoperative Pathologies Identified	
Mitral regurgitation 2° ruptured posterior chordae	4
Mitral regurgitation 2° elongated anterior chordae	4
Mitral regurgitation 2° annular dilatation	2
Atrial septal defect secundum	5
Aortic regurgitation	2
Calcific aortic stenosis	1
Ebstein's anomaly	1
Hypertrophic obstructive cardiomyopathy	1
Atrial septal defect primum	1
Total:	21

Results

Prebypass Evaluation: Twenty-one pathological entities were identified intraoperatively (Table 2), mitral regurgitation due to ruptured chordae of the posterior leaflet in four patients, elongated chordae of the anterior leaflet in four patients, and pure mitral annular dilatation in two patients. (Two patients had both anterior and posterior leaflet pathology [Fig. 1] and one patient had mitral regurgitation secondary to tight aortic stenosis but TEE indicated normal morphology.)

Associated aortic regurgitation due to prolapse of the noncoronary cusp was found in one patient and central regurgitation (later found to be due to fenestration) in the second patient. One patient was found to have atherosclerotic aortic stenosis.

Discontinuity of the atrial septum was detected in five patients, four patients with ostium secundum, one isolated case with partial anomalous venous drainage, and one patient with ostium primum defect (Fig. 2). Displacement of the septal leaflet with a large atrialized right ventricle and hypertrophic obstructive cardiomyopathy with a septal wall thickness of 2.7 cm was detected in the remaining two patients. The patient with hypertrophic obstructive cardiomyopathy had associated ostium primum atrial septal defect.

Surgical Treatment: Surgical treatment included quadrangle resection of the posterior leaflet of the mitral valve supported by Carpentier mitral ring in four instances for ruptured posterior leaflet chordae, chordal shortening and chordal transfer to the anterior leaflet in four instances for elongated anterior leaflet chordae, and Duran flexible ring in two instances for pure annular dilatation. Complete closure of the atrial septal defect with pericardial patch in four instances for atrial septal defect of secun-

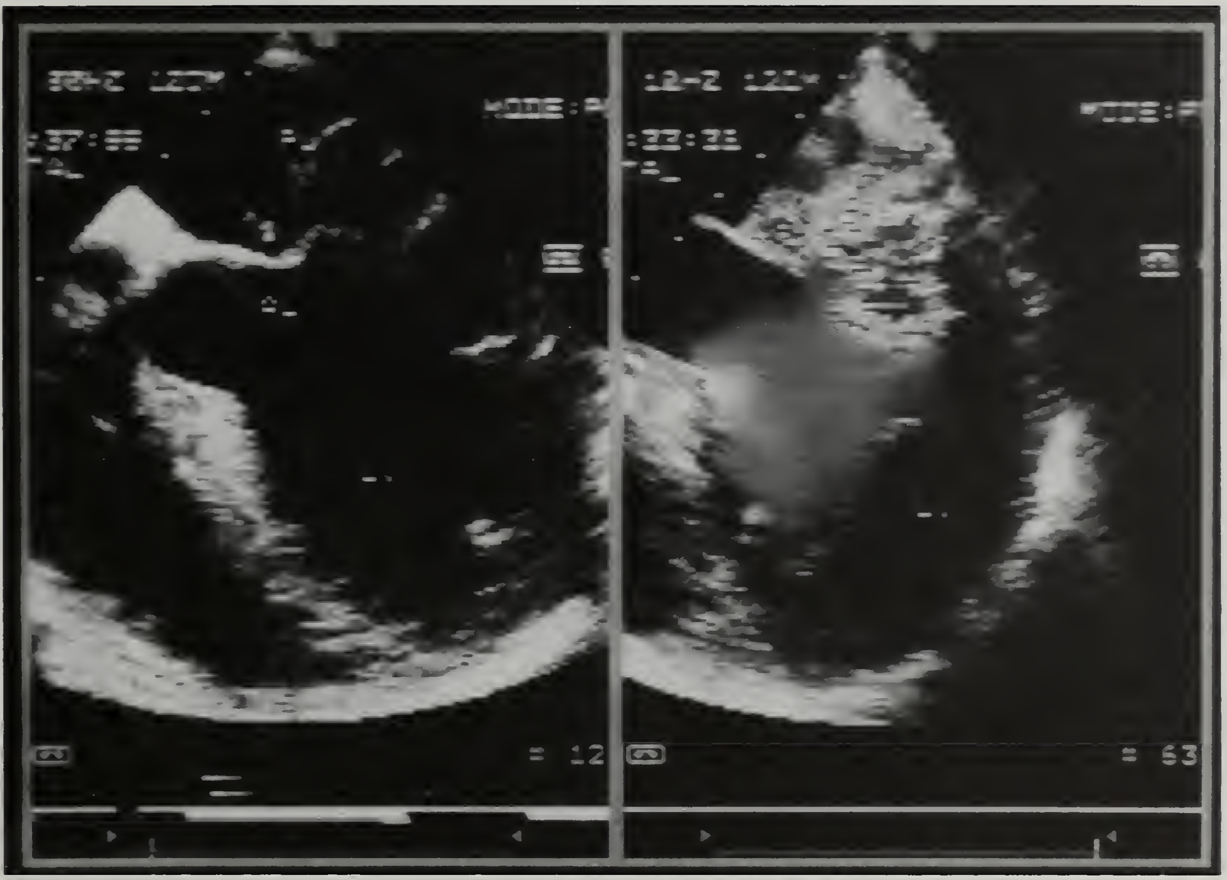

Figure 1

***Left Panel.* TEE of flail posterior leaflet (PL) and prolapse of the anterior leaflet (AL) of the mitral valve. *Right Panel.* Color flow imaging showing severe mitral regurgitation. LV = left ventricle.**

dum type, ligation of small partial venous drainage in one instance, a Dacron patch for ostium primum in one instance, and aortic valve replacement in two instances—one after an attempted aortic valve repair and second for calcific aortic stenosis. Aortic valve repair with resuspension of prolapsed noncoronary cusp in one instance, myomectomy for hypertrophic obstructive cardiomyopathy in one instance, and repositioning of the displaced septal leaflet to anatomical annulus supported by Duran flexible ring in one instance. TEE findings prevented mitral valve surgery in one patient with mitral regurgitation (normal valve morphology with mild regurgitation secondary to severe aortic stenosis).

Coronary bypass grafting was done in two patients with associated coronary artery disease.

Postbypass Evaluation: There was either no or trivial mitral regurgitation in eight patients (seven with repairs) (Fig. 3) and mild residual mitral regurgitation in one patient. This young patient had undergone attempted aortic valve repair for fenestration ending with aortic valve replacement. Chordal transfer was done for anterior leaflet elongation. The residual regurgitation was acceptable because of prolonged aortic cross-clamp time in this patient. All five atrial septal closures had intact septa with no residual shunts. There was trivial aortic regurgitation in the patients who had the aortic valve repair. There was no evidence of ventricular septal perforation in the patient who had undergone myomectomy for hypertrophic obstructive cardiomyopathy and a satisfactory reattachment of the tricuspid valve in Ebstein's anomaly with minimal residual tricuspid regurgitation. This could not be completely corrected because of tethered chordae of the anterior leaflet to the right ventricular cavity.

Discussion

Transthoracic echocardiography provided adequate images of the intracardiac structures. Obesity, emphysema, and chest wall deformity prevented good images by this approach[1] but the lack of discomfort in the patients was an important consideration. Sterilized transthoracic probes offered limited contact with the surface, cessation of monitoring during the surgical procedure, and caused multiple ventricular arrhythmias.

Since the introduction of TEE in 1971[2] and its clinical application[3] this modality investigative tool for intracardiac evaluation has gained in popularity. Because of its close approximation to the heart, this modality offers excellent imaging of the atrial septum, anterior and posterior mitral valve morphology and hemodynamics, aor-

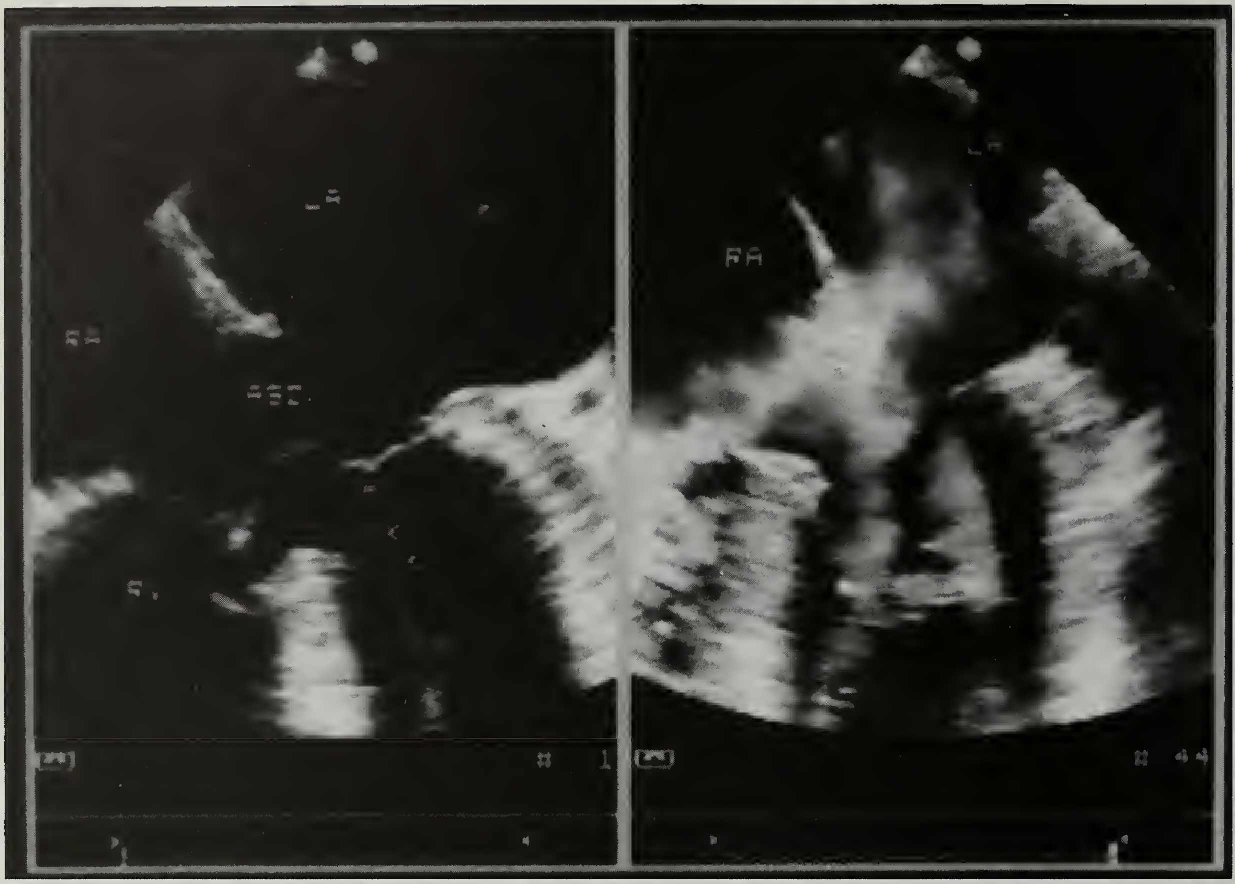

Figure 2

***Left Panel.* TEE four-chamber view shows an ostium primum atrial septal defect (ASD) and hypertrophic cardiomyopathy with systolic anterior motion (arrowheads) of the mitral valve. *Right Panel.* Color flow imaging demonstrating a left to right shunt. LA = left atrium; RA = right atrium; RV = right ventricle.**

tic valve, left ventricular outflow tract, and ventricular septum. The atrial septum, right ventricular cavity, tricuspid valve, atrial appendages, and even the proximal coronary arteries can be evaluated.

Intraoperative TEE in the anesthetized patient has gained popularity in the recent past.[4,5,6,7] Its continuous use during uninterrupted surgical procedure, assessing any residual air left in the intracavity chambers and comparing left ventricular function pre- and postoperative valve repair have added further dimension to its use in the operating room. The apex of the left ventricle, subpulmonic area of the right ventricle, and pulmonary valve are difficult to evaluate using a single plane transducer.

TEE has been utilized in the diagnosis of atrial septal defect,[8] flail mitral valve[9] and various congenital anomalies, ventricular septal defect, transposition of great vessels, aortic stenosis, single ventricle and Ebstein's anomaly.[10] Recently, its application in detecting abnormalities of cardiac valve prostheses[11] and aortic dissection[12] have been suggested.

Vocal cord paralysis[13] and Mallory-Weiss tear[14] have been reported secondary to the procedure.

A single plane of a section instead of biplane has limited the use of TEE to assess completely the intracardiac pathology in all chambers of the heart.[15] A biplane TEE and pediatric-size transducer are already being tested and employed.

In our experience, atrial septal defect with associated anomalous pulmonary venous drainage was difficult to diagnose because of the single plane of visualization of the atrial septum. Anatomical intact repair in one patient with quadrangle resection and chordae transfer for mitral regurgitation, TEE demonstrated trivial mitral regurgitation. Reinspection of the valve after placing the patient on cardiopulmonary bypass failed to reveal any anatomical deformity. Mitral valve was not replaced and the patient demonstrated no mitral regurgitation on physical examination or transthoracic echocardiography postoperatively. This indicated to us that transesophageal echocardiography is a very highly sensitive instrument and that trivial or even mild residual mitral regurgitation can be accepted as good surgical repair postoperatively.

In one patient with mitral regurgitation and a tight aortic stenosis, there was normal morphology of the mitral valve apparatus. TEE was helpful in preventing repair or replacement of the mitral valve. Following aortic valve replacement, the patient exhibited trivial mitral regurgitation intraoperatively.

Intraoperative TEE was also helpful in detecting large amounts of air in the intracardiac chambers, if present, prior to decannulation. Comparing the ejection fraction of the left ventricle from preoperative status, cardiotonic drugs were instituted at an early instance before cardiovascular collapse set in.

The present study was done in 14 consecutive patients with valvular and congenital anomalies in the adult population. This technique has helped us to achieve enough technical experience to enable us to employ it for routine use in more complex cases. TEE probably is not necessary in patients presenting with atrial septal defect of secundum type. Direct satisfactory complete closure with pericardial patch may obliviate the need for the postrepair evaluation in these patients.

The availability of biplane TEE in the future will be most beneficial to assess completely the mitral valve apparatus, to plan the modality of treatment, to choose the technical repair suited for that pathology, and to check the outcome of the operative procedure before disconnecticng the patient from cardiopulmonary bypass.

In conclusion, TEE permitted complete assessment of the mitral and tricuspid valve apparatus, atrial septum and aortic valve, and subaortic areas. It was also helpful in evaluating intraoperative valve repair and residual shunts, and prevented surgery on the mitral valve presenting as a mitral regurgitation secondary to critical aortic stenosis. The morphology of the mitral valve was found to be intact. TEE is an indispensable tool in valve reconstruction procedures and some congenital anomalies in the adult population.

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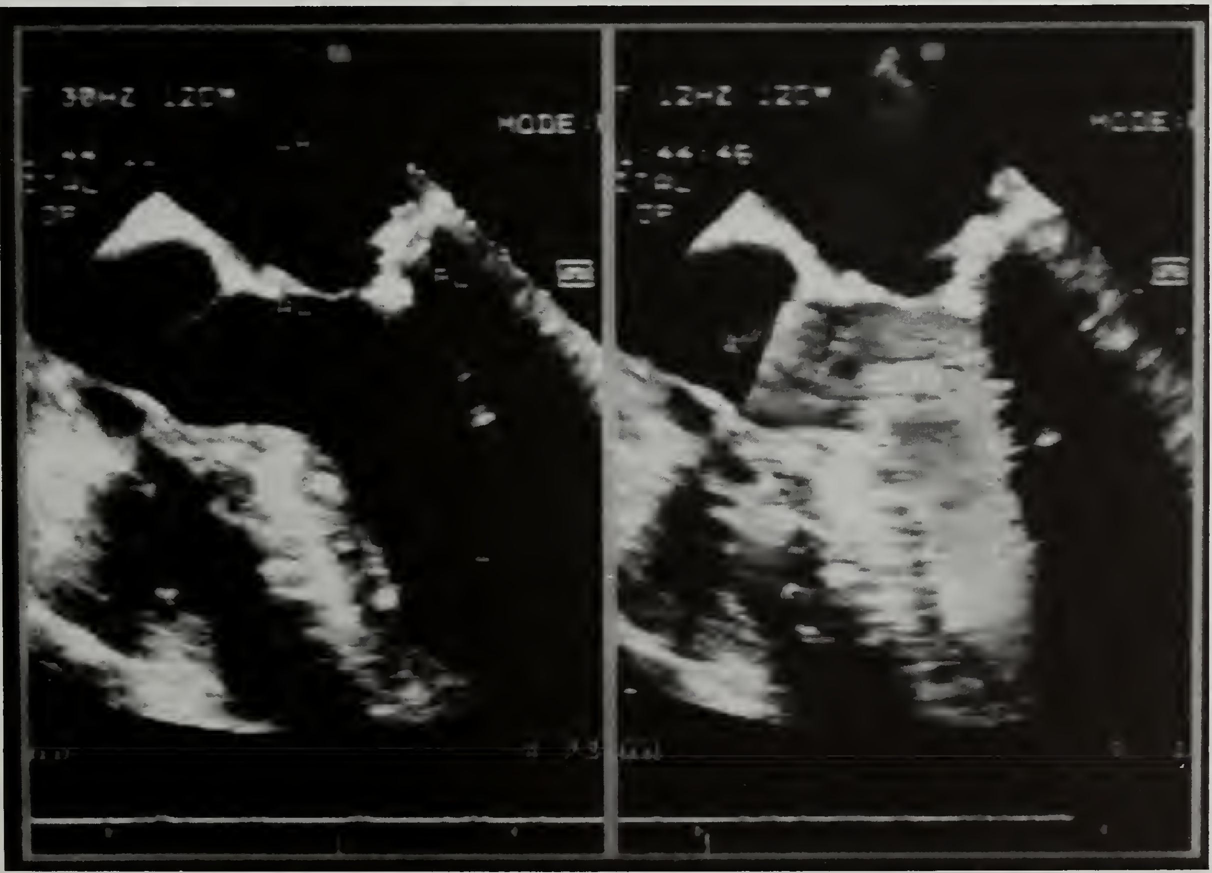
Figure 3

TEE following mitral valve repair (same patient as Fig. 1). *Left Panel.* A Carpentier annuloplasty ring has been placed and quadrangle resection of the posterior leaflet (PL) and chordal transfer to the anterior leaflet (AL) performed. *Right Panel.* Postrepair, there is no mitral regurgitation. LA = left atrium; LV = left ventricle.



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Physicians to Help Patients Quit Smoking

The Connecticut State Medical Society (CSMS) has cosponsored a "**How to Help Your Patients Stop Smoking**" workshops program for Connecticut physicians. The National Cancer Institute (NCI) and the National Institutes of Health (NIH) of the U.S. Public Health Service have developed these one-hour courses based on clear NCI findings that physicians who use these brief intervention techniques can have a significant impact on smoking rates among their patients. NCI's goal is to train 100,000 practitioners by the end of 1992. It is one part of NCI's effort to reduce U.S. cancer mortality rates 50% by the year 2000.

The program's cosponsor, the American Cancer Society, Conn. Division (ACS), (with support from NCI, NIH, AMA, CSMS, CAFP, UConn School of Medicine, and Yale Comprehensive Cancer Center), has already conducted a full-day session earlier this year to teach some 50 trainers how to conduct these workshops for their colleagues, and now it is time to put them to work.

CSMS has asked the Directors of Medical Education (DME) in each local hospital having accreditation from CSMS as a sponsor of continuing medical education (CME), to include one of these NCI workshops as part of their CME schedule this fall. ACS-Connecticut Division will arrange to provide speakers and NCI-supplied training materials for each workshop. The Cancer Society will also ask its local units' Medical Affairs Committees to promote attendance among nearby colleagues.

In addition, CSMS will widely publish the schedule of these meetings to provide maximum opportunity for doctors to attend one conveniently. CSMS and Group Health Cooperative of Puget Sound (GHC) will prepare media releases and public service announcements to support physician-directed smoking cessation, and will also collaborate in a research study to discern changes in physician attitudes and practices over the course of the project.

The State Medical Society is urging its 6,000 members to watch for the announcement of an NCI "**How to Help Your Patients Stop Smoking**" workshop at their local hospital or one nearby. It's one more way in which physicians can make a beautiful difference in the lives of their patients.

Recommendations on HIV Education, Counseling, and Testing for Women

SUSAN S. ADDISS, M.P.H., M.Ur.S.

THE number of AIDS cases among women in Connecticut has increased substantially in recent years. Twenty percent of AIDS cases in Connecticut residents have been in women, compared to a national rate of 10%. Many women who test positive for human immunodeficiency virus (HIV) are unaware of their risk of infection because they do not fall into "high-risk" categories. This growing problem in women warrants immediate attention by all health care practitioners. I am therefore asking you to increase your routine counseling and voluntary HIV testing efforts for women patients.

The infection rate among women of childbearing years is particularly alarming. For the past 18 months, the Department of Health Services has conducted a serosurvey of all newborn deliveries in the State of Connecticut. That survey, which tests the newborn's cord blood for HIV antibody and reflects the HIV antibody status of the mother, shows that 0.3% (one in every 333 births) are infected. It is estimated that 150 babies will be born to HIV infected women in 1991. Of these, it is expected that 45 babies will themselves be infected and at direct risk of the associated complications.

Twenty-five percent of the women reported with AIDS in Connecticut were exposed to the virus through sexual intercourse. Fifty-six percent were exposed through intravenous drug use. It is important to note that any woman can be at risk, including bisexual and lesbian women, who can be infected with HIV through injection of drugs with needle-sharing or through unprotected sexual intercourse.

Both New York State and New Jersey have recommended to physicians in their states that routine counseling and voluntary HIV testing be offered to women of childbearing age. Connecticut, which shares a serious HIV infection problem in women with these states, is now making similar recommendations.

HIV Education Counseling and Voluntary Testing: The Standard of Practice

Education and voluntary HIV antibody testing are important means of preventing HIV infection in women and preventing transmission of the virus to their children or sexual partners. The standard of practice in caring for women of childbearing age should include:

1. education about the virus and its transmission,
2. periodic individual assessment of risk behaviors and risk reduction counseling regarding drug use and sexual behavior, and
3. the offer of voluntary confidential or anonymous HIV testing to all women, especially pregnant women and women contemplating pregnancy.

Recent advances in treatment of HIV infection make identification of those who are infected especially important. Progression of immunodeficiency can be slowed and some opportunistic infections prevented if infection is detected and treated. In addition, women who are infected should be informed of the risk to their unborn children, especially in light of recent recommendations regarding prophylaxis for *Pneumoncystis carinii* pneumonia in HIV-infected infants. Infected women should also be offered the opportunity to notify their sexual and needlesharing partners.

Public Act 89-246, the AIDS confidentiality law, requires that HIV testing be done with both pre- and post-test counseling and the informed consent of the woman. Fear of discrimination, loss of confidentiality, and denial of medical care can be significant barriers to women who would otherwise want to know their serostatus. Counseling and testing sites funded by the Department of Health Services are available to women who are more comfortable seeking testing there. A list of those sites is available through the AIDS Section of the State Department of

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SUSAN S. ADDISS is Commissioner of Health, State of Connecticut Department of Health Services. This letter was sent to all physicians, nurses, and nurse practitioners in August 1991.

Health Services. Highly trained experienced counselors are available at these sites. Testing can be done either on an anonymous or confidential basis. If a release of information is obtained, the test results can be shared with the woman's health care provider. The woman may also be tested through her usual health care practitioner..

The Department of Health Services has a training program for health care providers who are interested in developing or enhancing health education, counseling, and testing skills. If you or your staff are interested in such training, please call Irene Mason or Richard Melchreit at 566-1802. Brochures for education of your patients can be obtained in English or in Spanish by calling 566-1157. The CARE Program is available for notification of partners of infected individuals and can be reached at 566-4493.

Recommendations

In summary, the Department of Health Services recommends the following:

1. Routine periodic assessment of risk behavior, counseling and voluntary HIV testing of all sexually active women, drug injecting women, and women of reproductive age. HIV risk assessment, counseling and testing should be routinely provided in primary health care, gynecological, family planning, prenatal and perinatal settings. Whenever possible, HIV risk assessment should be done and counseling and testing should be offered before pregnancy occurs and on at least an annual basis for those whose behavior continues to put them at risk. Guidelines are available through the AIDS Section of the State Department of Health Services.
2. Testing should be done with the written informed consent or documented oral consent of the patient, in compliance with Public Act 89-246. If a woman prefers, she can be referred to an HIV counseling and testing site from the list for confidential or anonymous testing below.
3. HIV infected women who are pregnant or are contemplating pregnancy should be counseled about the risks of pregnancy and transmission of HIV. Medical professionals should respect the HIV infected woman's right to make her own reproductive choices.
4. HIV results are not reportable to the Department of Health Services unless the patient is coinfected with TB. All HIV-related information should be handled as confidential medical information as required by Public Act 89-246.
5. If a patient tests positive for HIV antibody, the usual health care provider can and should continue to provide medical care. Consultations can be obtained from physicians experienced in caring for HIV infected patients.
6. Many women at risk for HIV infection are also at risk for hepatitis B infection, sexually transmitted diseases, and tuberculosis infection. Patients should be periodically evaluated for these conditions as well, especially when contemplating pregnancy or when pregnant.
7. Health care providers should use these recommendations to develop policies and in-service programs for all members of the health care team. This information should be shared with non-English speaking health and social service providers in their language of comfort.

Any questions or comments about these recommendations should be made to:

Richard Melchreit, M.D.
Medical Associate
Connecticut State Department of Health Services
AIDS Section
150 Washington Street
Hartford, Connecticut 06106
566-1802

AIDS Counseling and Testing Sites

Bridgeport Health Department	576-7469
Danbury Health Department	797-7900
Greenwich Health Department	622-6488
Hartford Gay & Lesbian Health Collective Community Health Services	236-4431
Hartford Health Department	722-6742
Hartford Hospital	524-7398
Hill Health Center (New Haven)	776-9594
Meriden Health Department	238-0017
Middlesex Memorial Hospital	344-9998
Middletown Community Health Center	347-6971
New Britain Health Department	224-2420
New Haven Health Department	787-6453
New London Health Department	447-2437
Norwalk Health Department	854-7979
Stamford Health Department	967-AIDS
Torrington Health Department	482-8141
Waterbury Health Department	574-6883
William Backus Hospital (Norwich)	823-6343
Windham Regional Community Council	423-4447
Women's Health Services (New Haven)	777-4781
Yale-New Haven Hospital AIDS Care Program	785-5303 (in-house referral only)

Thoughts About Listening

ALFRED HERZOG, M.D.

AS president of the Medical Staff, I represent the over 600 colleagues who, in various ways, have been involved in your education and training at Hartford Hospital. It is a tradition that my comments be brief and to the point, as well as something worthwhile to think about long after today. I promise you the former; only time will tell about the latter.

For most of you, you probably have more medical knowledge now and in some instances more sheer technical skills, than you will ever have again in your career. I would not presume to try to add to that today. Instead, I would like to leave you with some thoughts about listening, especially to whom to listen and to what to listen during your career in medicine.

You are all physicians and all of you, in some way, will deal with patients. Obviously, it will be important—especially if you want to be successful—to listen to your patients. That is obvious, you say, and it undoubtedly is. Then why is it, I ask myself, that the single most common letter or call of complaint I get about one of our colleagues (and fortunately I don't get too many of them) is because "Dr. X didn't listen to me!" Think about one of your busy days. It takes time to listen and time is your most precious commodity. A bit of advice, then. Please always leave yourself some extra time in your daily schedule to allow yourself to listen just "long enough."

There is one other kind of listening to your patients about which I would like to remind you. Please always listen for what your patient is not telling you. I am reminded of a middle-aged man I saw in consultation about six months ago. He had just been admitted because of a car accident, trauma to his chest, and had a history of cardiac disease. I listened to his concerns about his heart, his anxieties, and his anger about ending up here again. But all of this did not add up to the degree of his present turmoil. I finally said, "You know, I think we're missing something. I don't think you are worried about your broken ribs and heart trauma; I think you are worried about your broken heart." He just looked at me for about a minute, then began to cry. I learned and he learned—during the next four months of treatment—just how much more grieving he had to do about his son's death five years before in an automobile accident. So please listen for what your patient is not saying, and yet what he or she needs to talk about.

Many of you are already married and have children or have a significant other and most of you will, eventually, have a family. Please also save time to listen to them. They, your spouse, your significant other, your children, often your family of origin, represent your most important support system. And as we get busy in our practices and commitments to patients, to courses, to meetings, etc., they are often the easiest to slight. Each and every one of you who is successful at your career—and each one of you hopefully will be—will have to contend with being "married" to this very privileged career of medicine and to your family all at the same time. Please pay attention to that dialectic. Don't take your spouse or your kids for granted. The solutions to this vary greatly. My wife and I try to take at least 10 minutes a day (more if we can) to listen to the *other* person. You may have better solutions, but make sure you have one.

Lastly, and most importantly of all, take time out to listen to yourself. I mean that both in terms of your profession and your personal life. Professionally, listen to yourself to make sure that practicing medicine remains fun for you. Should that feeling stop, make sure you talk to somebody—your spouse, a good friend, even a professional listener. If you don't, that is when you run the risk of turning to the wrong "support" system like alcohol or drugs.

In the personal realm of your life, listen to yourself a lot. Remember, each and every one of us makes mistakes, be they in the way we mistreat a patient at times or mistreat a spouse, a child, or a friend. Admit it when that happens to you and admit it to the other person. Most of us are very forgiving if we are treated with respect. Listen to yourself as well and make sure you develop an interest, a hobby,

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ALFRED HERZOG, M.D., is a practicing psychiatrist, President of the Medical Staff, Hartford Hospital, and Clinical Professor of Psychiatry, University of Connecticut School of Medicine.

These comments were made at the Hartford Hospital House Staff Graduation Ceremonies, June 1991.

something outside of medicine. You need that so as not to let medicine become stale in your life. Also listen to good friends outside of medicine to whom you are simply Al, or Joe, or Jane, or Susan. Those kinds of special friends—along with a lover, a spouse—the kind of special friend whom we let listen to a piece of our soul (if you will permit me to call it that), these kinds of friends keep us honest, on track, and invigorated about life. Cultivate them and let yourself listen to them.

I probably stretched the limits of brevity. So, enough about listening. I would like to close by extending to you our congratulations and also our thanks.

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Valuable financial planning ideas are available direct to physicians through a new and unique product—**Fresh Advice**. Published by the American Medical Association and Planning Focus, Inc., a Redmond, Washington-based publisher of legal educational programs for businesses and their professional advisors, **Fresh Advice** makes the best in physician planning ideas available to you.

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Important Advances in Clinical Medicine

Allergy and Immunology

The Scientific Board of the California Medical Association presents the following inventory of items of progress in allergy and immunology. Each item, in the judgment of a panel of knowledgeable physicians, has recently become reasonably firmly established, both as to scientific fact and important clinical significance. The items are presented in simple epitome, and an authoritative reference, both to the item itself and to the subject as a whole, is generally given for those who may be unfamiliar with a particular item. The purpose is to assist busy practitioners, students, researchers, or scholars to stay abreast of these whether in their own field of special interest or another.

The items of progress listed below were selected by the Advisory Panel to the Section on Allergy and Immunology of the California Medical Association, and the summaries were prepared under its direction.

New-Generation Antihistamines

HISTAMINE$_1$-receptor antagonists have been the mainstay of the treatment of various allergic disorders for numerous years. Drowsiness from using traditional antihistamines, an effect attributed to the inhibition of histamine *N*-methyltransferase and the blockage of central histaminergic receptors, has limited the usefulness of this category of medication. In one survey, 62% of patients with significant upper respiratory tract allergy symptoms avoided using an antihistamine for relief because of the resulting sedation. Relatively nonsedating antihistaminic agents have recently become available. These new-generation H$_1$-receptor antagonists are lipophobic and penetrate the central nervous system to a lesser degree than their first-generation predecessors, thereby greatly decreasing their propensity to sedate. Other advantages of these new antagonists include preferential binding to peripheral H$_1$-receptors over central ones and the property of possessing minimal antiserotonin, anticholinergic, and α-adrenergic blocking activity.

The present list of second-generation H$_1$-receptor antagonists includes terfenadine, astemizole, loratadine, cetirizine, and azelastine. Only the first two antihistamines are currently available in the United States. Studies of these new agents reveal the incidence of sedation and performance have shown that the new-generation antihistamines are a substantial improvement over previously available antihistamines. Other adverse effects of these H$_1$-receptor antagonists have been reported, however. Terfenadine, at high doses or in combination with other drugs, may have rare cardiotoxic effects. Astemizole may occasionally stimulate the appetite and cause inappropriate weight gain. Large doses of astemizole may also result in cardiac rhythm irregularities. Astemizole binds to peripheral H$_1$-receptor sites with far greater affinity than any other existing H$_1$-receptor antagonist. A suppression of histamine-induced wheal-and-flare reactions may still occur in some patients as long as 14 weeks after discontinuing the medication.

Second-generation H$_1$-receptor antagonists have proved to be effective in decreasing symptoms of sneezing, itching, and nasal discharge, and ocular symptoms in most patients with allergic rhinoconjunctivitis. Challenge studies using intranasal antigen have shown this new category of antihistamines to block or attenuate the immediate reaction to a challenging allergen. Most evaluations show, however, that these agents are no more effective than first-generation H$_1$-receptor antagonists. The manufacturers recommend the following doses to provide optimal efficacy with a minimal likelihood of causing sedation or other adverse effects: terfenadine, 60 mg twice a day; astemizole, 10 mg daily; loratadine, 10 mg daily; cetirizine hydrochloride, 10 mg daily; and azelastine hydrochloride, 4 mg per day. Although studies comparing these new agents are limited, there is some

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information to suggest that terfenadine relieves symptoms more rapidly than astemizole, but astemizole may have a longer duration of action than the other new agents.

There is some interest in applying these new H_1-receptor antagonists topically to the nasal mucosa and conjunctivae. Studies using intranasal azelastine have shown substantial protection against allergen-triggered rhinitis and allergic conjunctivitis. These new agents may have antiallergic properties different from their H_1-blocking activity. That is, they may decrease the release of inflammatory mediators such as histamine and prostaglandin D_2 from mast cells and basophils, a property different from the simple antagonism of H_1-receptors. Because of these antiallergy properties, second-generation antihistamines have also been studied for beneficial effects in the treatment of asthma. Under controlled conditions in the laboratory, some of these new antagonists have clearly had a protective effect against bronchospasm induced by allergens, exercise, histamine, or cold air. Further studies are underway to investigate their possible beneficial effects in patients with asthma. Second-generation H_1-receptor antagonists have also been used in the treatment of chronic idiopathic urticaria, and results show them to be well tolerated and efficacious in modifying urticaria symptoms.

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Penicillin Allergy

FOR more than 50 years, the penicillins have been among the most useful antibiotics available for the treatment of human infections. The use of the penicillins and other ß-lactam antibiotics has been limited, however, by relatively high rates of allergic reactions among patients and the failure of physicians adequately to identify those patients who are at risk for such reactions. Treatment courses with penicillins are complicated by hypersensitivity reactions in as many as 10%, anaphylactic reactions in 0.01%, and fatal reactions in 0.0015%, or about 1 per 50,000 treatment courses.

Identification of the immunologic metabolites of penicillin has enabled a prospective identification of many patients at risk for systemic or potentially fatal type 1 immediate (IgE-mediated) hypersensitivity reactions to these antibiotics. In vivo, a small portion of administered penicillin is metabolized to biochemically active compounds that can covalently bind to plasma proteins and elicit immunologic responses. The penicilloyl product is the most abundant metabolite, accounting for 95% of protein-bound drug metabolites, and is thus termed the "major determinant." This determinant is commercially available for skin testing. Three other penicillin metabolites, termed the "minor determinants," consisting of penicillin, penicilloic acid, and penilloic acid may play an important role in penicillin allergy. Although not currently available commercially, they have been synthesized in several laboratories at academic centers.

Skin testing is simple, sensitive, and specific for predicting immediate-type hypersensitivity reactions to the penicillins. When testing is done by trained personnel, patients with a history of an adverse reaction to penicillin and negative epicutaneous and intradermal skin tests with major and minor determinants (and appropriate positive and negative controls) have less than a 1% risk of a subsequent IgE-mediated systemic reaction. Skin test reactions to any of the penicillin determinants carries about a 70% chance of systemic reactions when the drug is subsequently administered. The sensitivity of testing with the penicilloyl (major) determinant alone is only 76%, whereas the sensitivity of testing with the penicilloyl and benzylpenicillin determinants is approximately 93%.

In absence of available minor determinants, physicians have relied on the clinical history alone and the availability of alternative antibiotics. In one report, only 10% of patients with a history of penicillin allergy were found to have positive skin tests with both the major and minor determinants. As many as 90% of patients are thus unnecessarily deprived of a highly effective, nontoxic, often less expensive class of antibiotics. Some practitioners have suggested using "old" aqueous penicillin for skin testing, erroneously thinking that the aging process will lead to the formation of hydrolysis products that will cross-react with minor determinants; this is an unacceptable practice. It is hoped that the penicillin minor determinants will be commercially available in the near future.

Although cross-reactivity between cephalosporins and penicillin has been shown in many animal systems, the true in vivo incidence of such cross-reactivity is not known. Cephalosporin skin testing is limited to the native drug because the relevant degradation products are unknown, but the use of the native drug alone appears to have little predictive value. Ongoing prospective studies suggest that the incidence of cross-reactivity is probably low, but more accurate determination is needed. In studies to determine the level of allergic cross-reactivity between the monobactam antibiotics and the penicillins, there was no evidence of immunologic cross-reactivity. Moreover, to date, patients with a history of true IgE-mediated penicillin reactions have had no adverse reactions from monobactam antibiotics. Studies have also been conducted comparing skin test reactivity between the penicillin determinants and the major and minor determinants of the carbapenam antibiotic, imipenem. A high degree of cross-reactivity between the minor determinants of penicillin and the analogous determinants of imipenem was found, suggesting that this drug should be given to penicillin-allergic persons with the same degree of caution as if the patients were to receive penicillin.

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Points to Consider in the Care of Patients Infected With the Human Immunodeficiency Virus

As human immunodeficiency virus (HIV) disease is recognized more as a progressive chronic illness, primary care practitioners will be assuming more responsibility for the care of these patients. Practitioners need to be familiar with the initial staging of the disease, current health maintenance recommendations, and prophylaxis and treatment regimens.

The initial staging of HIV infection relies on the patient's history, pertinent physical findings, the CD4:CD8 cell ratio, and the absolute CD4 and CD8 cell counts. A history of opportunistic infections, malignant neoplasms, or wasting symptoms is important, but a history of tuberculosis, syphilis, or herpes simplex or zoster infections should also be obtained. A thorough travel history is important because disseminated coccidioidomycosis or histoplasmosis can be the initial presentation of an HIV-infected patient from an endemic area.

The initial physical examination should emphasize those findings that define the acquired immunodeficiency syndrome (AIDS) or the AIDS-related complex. The early signs of HIV dementia in particular can be subtle.

Once a person tests positive for HIV antibodies, laboratory studies should include a complete blood count, a chemistry panel, and T-cell subsets. Serologic tests should include a hepatitis panel, rapid plasma reagin (RPR) or VDRL, and a *Toxoplasma* titer. A standard purified protein derivative (PPD) and a control skin test should be administered. In asymptomatic patients, the T-cell subsets and complete blood count should be repeated every three to six months. The chemistry panel should be repeated every six months or more frequently if symptoms develop or if the patient is taking a hepatotoxic medication. The RPR and PPD tests should be repeated annually. Vaccinations have been found to be variably effective in HIV-infected persons: the pneumococcal vaccine should be given once, a conjugate influenza vaccine annually, and hepatitis B vaccine if results of the hepatitis panel are negative.

The only anti-HIV therapy that is approved by the Food and Drug Administration at this time is zidovudine (AZT). This nucleoside analogue selectively inhibits HIV type 1 reverse transcriptase activity and viral replication. Two recent clinical trials have shown that the development of AIDS or severe AIDS-related complex is substantially delayed in patients taking AZT. In addition, the use of AZT has been shown to have significant therapeutic effects in patients with AIDS dementia. It is generally recommended to begin AZT therapy in all HIV-infected patients with CD4 counts of less than 0.5 cells X 10^9 per liter (500 cells per μl). Some argue that this increases the risk of drug resistance developing, however. Recent clinical trials have shown that decreasing the dose from 1,500 mg per day to 500 per day (100 mg every four hours) offered asymptomatic patients clinical benefit with substantially fewer toxic effects. Another dideoxynucleoside analogue, dideoxyinosine (DDI), is presently undergoing a clinical stage II-III trial. Studies show it has potent anti-HIV activity, but it also has significant toxicity, some of its effects including peripheral neuropathy and pancreatitis.

The US Public Health Service recommends *Pneumocystis carinii* pneumonia prophylaxis for all patients with CD4 counts of less than 0.2 X 10^9 per liter (200 per μl). The combination drug, trimethoprimsulfamethoxazole, 5 mg per kilogram per day in a divided dose for three days a week, is one regimen. Unfortunately, there is a relatively high incidence of sulfa sensitivity in patients with AIDS. The use of dapsone, 50 mg per day, is an acceptable alternative that has not been studied as carefully. Aerosolized pentamidine given as a 300-mg dose every month was shown to decrease the number of episodes of *P carinii* pneumonia and prolong survival. There have been a few reports of extrapulmonary *P carinii* in patients receiving aerosolized pentamidine treatments. Pulmonary relapses in this population tend to be in the upper lobes.

Mycobacteria, both typical and atypical forms, have a strong association with HIV infection. The Centers for Disease Control recommend that any HIV-positive person, regardless of age, who has a positive PPD skin test (5 mm of induration) take isoniazid, 300 mg per day, for about a year. Currently there is no accepted prophylactic regimen for atypical mycobacteria.

Recurrent herpes simplex virus 1 and 2 and herpes zoster infections can be prevented with the use of acyclovir, 200 mg three to four times a day. The routine use of acyclovir or ganciclovir in an effort to prevent symptomatic cytomegalovirus infection is not recommended.

Persons infected with HIV who have a positive RPR or VDRL should have a lumbar puncture study done. If cerebrospinal fluid (CSF) is normal, the patient may be treated with 2.4 million units of penicillin G benzathine given intramuscularly weekly for three weeks. If there are typical symptoms of neurosphilis or if the CSF VDRL is positive for syphilis, treatment should be started. Many HIV-infected persons have an increased CSF protein concentration and pleocytosis, so these findings alone do not implicated neurosyphilis.

Human immunodeficiency virus disease should be considered a progressive, chronic process. Primary care practitioners need to lay the foundation for the care of HIV-positive patients. Patients can manifest a spectrum of diseases, many of which may now be preventable. Checking serial CD4 counts and getting careful interval histories and physical examinations will enable physicians or allied health care practitioners to stage the disease and plan appropriate maintenance measures.

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Harmful Health Effects of Passive Smoking

ALTHOUGH the role of direct cigarette smoking in chronic diseases including lung cancer and heart disease has been well established, scientific evidence has only recently implicated the indirect inhalation of cigarette smoke as a risk factor for disease as well. Since the Surgeon General's 1986 report on involuntary smoking, several hundred scientific articles have reported the harmful effects of environmental tobacco smoke. The Environmental Protection Agency recently called environmental tobacco smoke "one of the most widespread and harmful indoor air pollutants."

The strongest evidence linking passive smoking to increased disease prevalence exists in children. Even in temperate climates, children spend about two thirds of their time indoors, placing family members living with smokers at increased risk. It is estimated that 70% of all children in the United States are exposed to the hazards of cigarette smoke for much of their developmental years. During the first year of life, pneumonia and bronchitis appear with greater frequency in infants with exposure to cigarette smoke. There is also an increased incidence of otitis media, bronchitis, acute exacerbations of asthma, and reduced lung function in children whose parents smoke. Cough and mucus production occur more frequently among children of smokers. These clinical problems often have a dose-response relationship whereby the more cigarettes per day the parents smoke, the more likely a child is, for example, to require asthma medications. In addition, an increased serum immunoglobulin E level and an increased prevalence of eosinophilia have been seen among children of smoking parents. This may explain in part the increased frequency of respiratory symptoms in children of smoking parents. Furthermore, children whose parents smoke are twice as likely to become smokers themselves, additionally jeopardizing their health in later life.

The risk of environmental tobacco smoke to adults has not been examined extensively and is therefore not conclusive. One startling finding is that passive smoking is associated with a higher risk of lung cancer in nonsmokers. The National Academy of Sciences (1986) estimated that 3,800 lung cancer deaths each year in the United States are caused by passive smoking. Studies examining respiratory symptoms in adults with exposure to secondhand smoke have shown conflicting results, as have others examining lung function and clinical exacerbations of asthma. Those living with smokers are not the only ones at risk. A health insurance survey concluded that almost two thirds of nonsmoking adults had some exposure to passive smoke, most often in places outside the home. Testing for urinary or salivary levels of cotinine, a by-product of cigarette smoke, has documented the presence of tobacco smoke exposure in a large proportion of the general population.

Secondhand smoke is now recognized as a health threat in this country. This has caused a dramatic change in public attitudes regarding the rights of the smoking minority versus the welfare of the nonsmoking public. Further research is needed to determine more precisely how great the risk is from this exposure.

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Immunoglobulin G Subclasses

THE four immunoglobulin (Ig) G subclasses are products of discrete constant region genes encoded within the immunoglobulin heavy-chain locus on chromosome 14. Each immunoglobulin represents the expression of several rearranged variable region genes with one constant region gene producing a single polypeptide chain. The finished immunoglobulin molecule is a four-chain structure composed of two identical heavy chains coupled to two identical light chains (χ or λ) encoded on chromosomes 2 and 22, respectively. Monoclonal antibody and recombinant genetic technology have resulted in major advances in understanding immunoglobulin structure-function relationships as well as accurate methods for measuring IgG subclasses and specific antibodies to defined antigens.

Studies of purified isolates of human IgG subclasses, or genetically constructed antibodies of identical variable regions (idiotype) but different constant regions (isotype), have supplemented and clarified earlier studies of naturally occurring antibodies. These studies confirm major effector differences in IgG subclass antibodies. IgG3 is more efficient than IgG1 in activating complement, but IgG2 is minimally active and IgG4 is inactive. IgG1 is more efficient than IgG2 in enhancing human complement-mediated killing of some bacterial pathogens. IgG4 is functionally univalent and does not form large latticed immune complexes. Although these differences may have clinical implications, extrapolation from in vitro studies to defense capabilities in vivo may be misleading because of the physiologic redundancy of defense mechanisms.

Minor IgG subclass deficiencies have been linked to an increased susceptibility to infection. Often IgG2 or IgG2 to IgG4 deficiency occurs along with IgA deficiency. The strongest disease association has been that of low IgG2 levels and recurrent infection with encapsulated bacteria such as *Haemophilus influenza* type b and *Streptococcus pneumoniae*. The clinical implications of low IgG subclass levels are not well understood, however. Healthy persons lacking constant region genes for one or more IgG subclasses have been identified; healthy blood donors with variable IgG subclass deficiencies have also been found; persons with initially low IgG subclass levels can correct over time; and, finally, normal IgG subclass levels but deficient specific antibody responses have been described in persons with recurrent infection. Thus, IgG subclass deficiencies are likely markers of broader immune abnormalities rather than inherent causes of disease. The best understood example of this is also IgG2 deficiency. Low IgG2 levels in patients with recurrent infection are associated with an inability to respond to bacterial polysaccharides, but in healthy IgG2-deficient persons, normal antibody responses are seen. This suggests that the primary defect is specific immune responsiveness to bacterial polysaccharies; if impaired, low IgG2 levels are frequently but not invariably found. Therefore, the assessment of recurrent sinopulmonary or systemic pyogenic infection—the major indication for evaluating IgG subclasses—should include both IgG subclass levels and specific antibody responses to protein and polysaccharide antigens, including the paired measurement of serum before and four weeks after immunization with capsular vaccines such as unconjugated *H influenzae* type b and pneumococcal polysaccharide vaccine. Age-related interpretation is essential because healthy infants and toddlers may not respond to these vaccines. At present, IgG subclass-specific antibody assays are not generally available. An IgG subclass deficiency associated with impaired antibody responses can be treated with intravenous immune globulin if conservative measures such as antibiotic prophylaxis are ineffective. The use of intravenous immune globulin therapy in patients with an IgG subclass deficiency without a demonstrably impaired antibody response is controversial; many clinicians await the results of a multicenter controlled trial now in progress.

An analysis of IgG subclass levels must take into account their non-Gaussian distribution, wide normal ranges, and ethnic differences. Allelic population differences in certain heavy- and light-chain regions (allotypes) can affect IgG subclass levels and specific antibody responses. For example, whites with the IgG2m(n) allotype have higher IgG2 levels and antibody responses to bacterial polysaccharides than persons lacking this allele. Adult levels of IgG1 and IgG3 are attained earlier then levels of IgG2 and IgG4. For IgG3 and especially for IgG4, true deficiencies are hard to establish, given that low levels are found in many normal younger children.

Generally, antibody responses to protein antigens—such as viral envelopes—mainly involve IgG1 and IgG3. Antibody responses to capsular polysaccharies seem to fall into two groups, those eliciting greater IgG2 isotype restriction such as *S pneumoniae* and those with a lesser degree of IgG2 restriction such as *H influenzae* or meningococcal types A and C, where substantial IgG1 responses may occur. Finally, antibody responses to protein antigens presented repetitively, such as allergen extracts used in hyposensitization therapy, are largely restricted to IgG1 and IgG4,with the latter often predominant.

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Eosinophilia-Myalgia Syndrome

THE presence of peripheral eosinophilia (an absolute eosinophil count of greater than 0.35 X 10^9 per liter [350 per µl]) provides a clue to an underlying allergy, parasite infection, the pulmonary infiltrates and eosinophilia syndrome, a neoplasm, vasculitis, an immunodeficiency state, and idiopathic hypereosinophilic syndrome, or a drug reaction. The diagnosis of a drug reaction is usually based on the response to removing the drug and the exclusion of other possible diagnoses, as drug reactions have no pathognomonic clinical or laboratory findings. The association of the eosinophilia-myalgia syndrome (EMS) with the ingestion of the amino acid tryptophan is a striking, newly recognized example of a drug reaction associated with eosinophilia. In response to this association, the Food and Drug Administration banned all over-the-counter sales of tryptophan in December 1989.

The current surveillance definition of EMS used by the Centers for Disease Control (CDC) requires the fulfillment of three criteria: an eosinophil count of greater than 1 X 10^9 cells per liter (1,000 cells µl), incapacitating myalgias, and the exclusion of other infectious and neoplastic causes. In addition to the prominent muscle involvement (myalgias and muscle tenderness), the other organs involved in EMS include the skin (edema of the skin, transient maculopapular or urticarial rash and late morphealike lesions), lungs (dyspnea, cough, hypersensitivity pneumonitis), heart (palpitations, myocarditis), joints (arthralgias), and peripheral nerves (paresthesia). Although creatine kinase levels are usually normal, aldolase levels are frequently elevated, and a muscle biopsy specimen shows perivascular infiltrates of eosinophils and mononuclear cells. Patients with EMS have degranulated eosinophils in affected tissues, widespread activation of collagen gene expression in dermal fibroblasts, and increased tryptophan metabolism by way of the kynurenine pathway.

Available in the United States since about 1974 as a dietary supplement without prescription, tryptophan has been a popular remedy for insomnia, the premenstrual syndrome, depression, and loss of weight. Average doses or tryptophan range from 1 to 5 grams per day. In comparison, single servings of meat, fish, poultry, and some cheeses contain more than 200 mg of tryptophan. Tryptophan is metabolized by way of hydroxytrypophan to serotonin or by an alternative pathway to kynurenine. Because tryptophan is an essential amino acid, the presence of a contaminant or impurity in tryptophan products has been postulated to be responsible for the syndrome. In Minnesota, an analysis of the epidemiology of EMS has revealed that the outbreak of EMS was associated with the consumption of tryptophan manufactured by one of six manufacturers providing tryptophan to US consumers before December 1989. Even though the purity of tryptophan in the company's manufacturing process was at least 99.6%, a trace contaminant formed after a chemical reaction between two tryptophan molecules and acetaldehyde (1, 1' -ethylidenebis [tryptophan]) has been associated with the risk of EMS developing.

At least 19 deaths and more than 1,400 cases of severe inflammatory disease due to EMS have been reported to the CDC. While the current CDC surveillance criteria for the diagnosis of EMS may exclude patients with milder forms of the syndrome, caution should still be exercised in diagnosing EMS in patients without eosinophilia because various rheumatic diseases, including fibrositis, polymyalgia rheumatica, and systemic sclerosis, may produce similar clinical manifestations. Therefore, the diagnosis of EMS in patients with milder myalgias, lower eosinophil counts, or other features suggestive of EMS requires clinical judgment and the appropriate weighing of all available clinical, laboratory, and, where indicated, muscle biopsy information. Because the only clear-cut recommendation for therapy (to stop ingesting tryptophan) has already been made, the use and the duration of other therapies, such as glucocorticoids, needs to be tailored to each patient, depending on the severity of the disease and risk-benefit considerations.

Although further studies may provide important insights into the cellular mechanisms of action of the postulated trace contaminant responsible for EMS, the identification of tryptophan as the etiologic agent associated with the development of EMS and its prompt removal from the over-the-counter market has prevented EMS from becoming an even greater public health concern.

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Asthma Without Wheezing

ASTHMA is a disorder characterized clinically by episodes of wheezing, dyspnea, cough, and chest tightness. Spirometry shows reversible airways obstruction, but asthma may present with dry cough as its sole manifestation. This form of asthma has been variously termed "hidden," "atypical," "variant," or "cough-type" asthma. It appears to be a distinct disorder and is characterized by a dry, repetitive cough occurring during waking as well as sleeping hours that may be exacerbated by respiratory viral infections, exercise, and cold air. Frequently members of the immediate family have a history of allergy. Although found in all ages, atypical asthma is thought to be among the most common causes of chronic cough in childhood.

The cough of asthma is unresponsive to antitussives, antibiotics, and antihistamines, but it usually responds to a course of bronchodilators or corticosteriods. Routine spirograms may be normal. The diagnosis can be confirmed by a positive methacholine or exercise challenge test. The bronchial hyperresponsiveness evidenced by these tests is mostly reversed by the use of bronchodilators. In time, many patients have progression to typical asthma. In the differential diagnosis, other sources of cough should be considered, including the central nervous system and the pulmonary interstitium. Conditions such as pertussis, psychogenic cough, cystic fibrosis, sinusitis, and drug reactions are usually readily excluded.

One reason cited for cough without wheezing is that cough receptors are separate from the irritant receptors, which are responsible for wheezing. In one study the predominance of cough in a group of patients with asthma was attributed to cough receptors stimulated in the trachea and large bronchi where their number exceeds those in the smaller airways. In addition, mediators of asthma may have selective effects on the bronchial cough receptors.

Some authorities suggest that wheezing is present subclinically and would be uncovered with careful auscultation after maximal forced expiration. Wheezing after such maneuvers could not, however, be correlated with tests of bronchial hyperresponsiveness in a group of patients diagnosed as having atypical asthma.

Recognizing this form of asthma is important because the disorder responds readily to the use of bronchodilators in most patients and to corticosteriods in the rest.

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Chronic Granulomatous Disease

CHRONIC granulomatous disease (CGD) is a rare inherited disorder characterized by recurrent pyogenic infections, commonly involving the lung, liver, lymph nodes, or deep subcutaneous tissues. Chronic inflammation often develops, and complications due to obstructive granuloma, fibrosis, bronchiectasis, and emphysema may occur. Chronic granulomatous disease occurs because of an inability of phagocytic cells to convert oxygen into superoxide (0_2^-). The killing of ingested microbes is impaired because O_2^- is the precursor for all other microbicidal oxidants produced by phagocytic cells. The microorganisms most frequently responsible for infections in CGD include *Staphylococcus aureus*, *Enterobacter* species, and aspergilli.

An enzyme referred to as the respiratory burst oxidase is normally responsible for the generation of O_2^- and is defective in patients with CGD. The nitroblue tetrazolium (NBT) test remains the most common method to diagnose CGD. This test is based on the ability of O_2^- to reduce NBT from a yellow water-soluble tetrazolium dye to a blue insoluble formazan pigment that is easily visible under light microscopy as intracellular precipitates within activated neutrophils and monocytes. Recently it has become apparent that the oxidase is actually a complex multicomponent enzyme system that includes several cytosolic components and a unique heterodimeric membrane-bound cytochrome *b*. It is therefore not surprising that CGD, like many other inherited diseases, is a heterogeneous group of disorders, each with a different genetic defect affecting a separate component of the oxidase.

The discovery of a method to activate the oxidase in a cell-free system has made it possible to classify CGD into oxidase defects involving either the membrane or cytosol. Most patients with CGD (55% of cases) have a membrane defect due to abnormalities in the 91-kd glycoprotein subunit of the cytochrome *b*. The gene encoding this protein is located within the p21 locus of the X chromosome, and mutations at this site are responsible for the classic X-linked form of CGD. In 5% of cases, a membrane defect occurs due to an inherited abnormality in the 22-kd subunit of the cytochrome *b*, which is encoded by a gene on chromosome 16. No patients with CGD have been reported to have membrane defects other than abnormalities involving cytochrome *b* subunits. Patients with CGD who have cytosol defects (35% of cases) usually lack a 47-kd phosphoprotein. This protein is critical in the translocation of known cytosolic oxidase components to the membrane where the active oxidase resides. In 5% of cases, the CGD phenotype results from a deficiency of another cytosol oxidase component, a 67-kd polypeptide of unknown function. So far, all CGD patients with known cytosol defects have abnormalities involving either the 47-kd or 67-kd cytosolic proteins. Inheritance for both is autosomal recessive; the 47-kd and 67-kd proteins are encoded by genes on chromosome 7 and 1, respectively. The exact nature of the genetic defects causing these types of CGD remains unknown. Asymptomatic carriers of these cytosol defects can be identified using the cell-free system.

The cornerstones of therapy for CGD remain daily antibiotic prophylaxis, the early institution of parenteral antibiotic therapy, and the prompt surgical drainage of abscesses. Although no controlled trail has been done, extensive clinical experience has shown that antibiotic prophylaxis in patients with CGD reduces the incidence of infections and prolongs patients' survival. Recombinant human interferon gamma (IFN-γ) can now also be included as an effective and safe form of prophylactic therapy for patients having CGD. In a recently reported double-blind placebo-controlled study of 128 patients with CGD, recombinant IFN-γ therapy (0.05 mg per m^2 per dose given subcutaneously three times a week) led to a 70% reduction in the incidence of serious infections. Recombinant IFN-γ therapy was particularly beneficial in children younger than 10 years. The treatment was well tolerated in patients of all ages, and many patients treated for more than two years have yet to experience serious toxic effects. The clinical response to recombinant IFN-γ therapy occurred in all forms of CGD, regardless of the genetic defect, and was not associated with any improvement in phagocyte O_2^- production. The precise mechanism(s) of action of recombinant IFN-γ in CGD remains unknown; it appears that it enhances host defenses through a pathway other than phagocyte O_2^- production. Currently it is recommended that recombinant IFN-γ, three times a week, and daily antibiotic prophylaxis be given together indefinitely.

Based on the current understanding of the oxidase, it appears that somatic gene therapy directed at autologous marrow stem cells may eventually become a promising treatment of CGD. Further characterization of the oxidase also has important implications for disorders other than chronic granulomatous disease. It is anticipated that in the near future, agents that modify oxidase activity will become important anti-inflammatory drugs.

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New Uses of Intravenous Immune Globulin Therapy

ALTHOUGH the main indication for intravenous immune globulin (IGIV) is the treatment of primary immunodeficiencies, recent studies have shown a role for IGIV in treating selected secondary immunodeficiencies and autoimmune diseases.

Secondary immunodeficiency occurs in previously immunocompetent persons as a result of another disorder. Such disorders include prematurity, thermal and blunt trauma, leukemia, bone marrow transplantation, and human immunodeficiency virus (HIV) infection.

Data from several recent studies indicate a decreased risk of group B streptococcal infections in premature infants treated prophylactically with IGIV. Further studies are being done to help better define guidelines for the use of IGIV in these infants. Bone marrow transplant recipients treated with IGIV have reduced rates of septicemia and a decreased incidence of graft-versus-host disease compared with untreated controls. Intravenous immune globulin is also effective in decreasing serious bacterial infections in patients with chronic lymphocytic leukemia and hypogammaglobulinemia. Severe head trauma is associated with diminished antibody responses, and, because of this, the usefulness of IGIV in pediatric head trauma is currently under study.

Initial uncontrolled studies suggest a role for IGIV in patients with the acquired immunodeficiency syndrome, especially in young children who are antibody deficient and lack memory B cells. Until the results of controlled trials are available, the use of IGIV in patients with HIV infection remains controversial.

The treatment of both acute and chronic immune thrombocytopenic purpura with IGIV is now well established. This success has led to the investigation of its use in other autoimmune disorders. High doses of IGIV given within ten days of the start of Kawasaki's disease have been shown to decrease the incidence of coronary aneurysms and to reduce fever and acute inflammation. Recent studies have shown that a single large dose of IGIV, 2 grams per kilogram, is as effective as the previously recommended smaller daily dose given over four days. Other autoimmune diseases treated with IGIV include autoimmune hemolytic anemia, autoimmune neutropenia, myasthenia gravis, lupus erythematosus, rheumatoid arthritis, bullous pemphigoid, and diabetes mellitus. Most of the reports to date are anecdotal or are of preliminary uncontrolled trials.

The mechanism of IGIV action in autoimmune disease remains unknown. There is evidence in immune thrombocytopenic purpura that one mechanism may be Fc-receptor blockade. In Kawasaki's disease, the use of IGIV suppresses polyclonal immunoglobulin synthesis and T-cell activation. Another possible mechanism is immune network modulation by anti-idiotype antibodies present in IGIV. Elucidating the mechanism of this agent in these disorders will provide insight into the primary disorder itself that perhaps will lead to more specific and less costly therapies.

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Editorial

Guest Editorial

Is the Jury System or the Contingency Fee System Wrong?

Comments on the book *Jury of My Peers* and on our legal system.

Dr. Howard Snider's book is the story of a malpractice suit;[1] it was written by a surgeon who endured the stresses of a malpractice suit after he had done his level best for his patient. After the ordeal he had enough stamina left to write the story for us in an engaging style and to go even further, to research our legal system, trying to come to grips with the causes of the malpractice crisis and our "suit crazy society."

The book is fascinating not only for doctors but for everyone who is interested in medical, legal, and human affairs. Dr. Snider explains the medical aspects of the case in lay terms, lets us know about the functioning of our tort system as he himself becomes enlightened, and bares his own feelings in trying to understand the motivations and personalities of friends and foes in these dramatically personal events.

His case was a rare complication of heparin therapy that led to the disability of the plaintiff, yet not the plaintiff's attorney, not even his expert witness, and subsequently not even the jury ever knew this fact during the trial. The reasoning by the defense for not revealing this fact during the trial makes one wonder how justice can be served without the truth being revealed.

Change Needed

Dr. Snider came to the conclusion from his study of the American and other legal systems that our legal system needs a change. In this he is not alone. He quoted from George Wallace, a former judge: "Trial lawyers are getting fat and everybody else is paying through the nose.... This is not just a medical problem. It is not just a business problem. It is everybody's problem because it is the people that have to pay for it in the long run." Indeed, few people realize that the cost of prevention of litigation, the costs of litigation itself and of the huge awards to plaintiffs and trial attorneys come out of everybody's pocket as these costs are included in the price of goods and services we buy. Dr. Snider quotes Robert Browning, "something is wrong, there needeth a change," but it is not easy to see what change is needed and how can we achieve it.

In the following I will comment on Dr. Snider's conclusions and add some thoughts on the subject of the kind of tort reform needed to eliminate the liability crisis.

Patchwork of Legislations to Alleviate the Crisis

The malpractice crisis and the liability crisis have created a patchwork of legislation and proposals, state by state, to limit awards, to set up screening panels, to limit contingency fees, to make changes in procedure, to limit the liability of municipalities and schools and some other organizations, to cap punitive awards, and even to set up a no-fault system. All this has been to blunt the malpractice crisis and suit craziness; most of these legislative proposals were opposed by trial lawyers on constitutional grounds. Recently the Bush administration espoused further significant tort reforms at the state level, but we need to aim at the cure not just the alleviation of symptoms of the malpractice crisis.

Are Fickle Juries the Cause of Our Suit-Craziness?

Dr. Snider thinks that the cause of all this lies in our jury system, because juries have difficulty following scientific and highly technical aspects of the case, and because the jurors act and grant awards out of sympathy, regardless of the culpability of defendants. No doubt there are examples of such jury decisions, but there are also examples of rational decisions by juries in spite of aggressive plaintiff lawyers, and in criminal cases by overzealous or politically motivated prosecutors.

All in all, it is generally believed that jury decisions are unpredictable and that the whole justice system is characterized by mind-boggling inconsistencies. Trial lawyers often use this threat to induce the defendant to settle, even if the suit has little or no merit.

England has never been plagued by a liability crisis or suit-craziness, yet the jury system was abandoned there in tort liability cases in the 1920s for exactly the above reasons. The jury system, per se, did not produce a suit-craziness in England, therefore we have to look for the reason in some feature of the legal system unique to our country. One has to conclude that the driving force that has brought about the liability crisis, that has changed the interpretation of law and justice, and indeed the fabric of our society is the contingency fee system (CFS).

To the best of my knowledge, a financial interest by the plaintiff's counsel in the outcome of the trial has been considered unethical by all cultures and legal systems throughout history, and was not generally accepted as being ethical in the United States until the second half of the nineteenth century.[1] The introduction of the contin-

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gency fee system, not trial by jury, led to the development of suit-craziness in our society.

If the intent of the CFS was to enable the poor to sue, then the application of the system went far off course from its original intent. Now it is still difficult for the poor to sue for a just cause if the lawyer sees insufficient reward, and conversely the lawyers may steer the client into a contingency arrangement when the case seems promising even if the plaintiff would be able to pay the customary fee for services rendered in the case. Plaintiffs are quite satisfied with this arrangement because they do not have to pay in advance and because they feel that a better representation can be expected on a contingency basis. This is probably true, and brings us to the subject of unequal representation as will be discussed later.

Development of Deep Pocket Justice

When trial lawyers were guaranteed a cut of the award, they began to increase the amount of claims for real and undefinable damages, and more importantly, they convinced the courts to hold liable the party most able to pay rather than the one most culpable. This is how "deep pocket" justice started to take hold, which in turn increased the fear of liability, leading to ever increasing liability insurance premiums, creating new and deeper pockets for the trial lawyers to dip into. At the same time spectacular awards fueled a greed in our society, in all of us, by an expectation that some misfortunes could be converted into fortunes by the courts, if a "deep pocket" could somehow be involved in the chain of events. Over time our legal system, our insurance system, and the way of thinking of our people were transformed into powerful machinery for making our trial lawyers rich, incidentally rewarding some plaintiffs handsomely along the way, while the awards to other plaintiffs melted away as legal costs and the contingency fees were deducted. Interestingly the portions of the award distributed to plaintiffs and their lawyers are seldom reported in the press, resulting in little public awareness of this aspect of the contingency fee system.

Dr. Snider cites several examples of sympathy awards, shifting of liability to the deep pocket, and disregard of technical evidence or even common sense in liability cases. One reads this in disbelief, but the daily papers reaffirm that these are not rare occurrences. *Newsday*, of Long Island, reported that on 14 September 1990 a 61-year-old woman was awarded $747,000 because she became blind after radiation therapy for a brain tumor. Without the treatment she would have died and all the medical experts who testified in the trial said that the procedure performed by the hospital was right. The jury was not available for comment. This appears to be a case of a sympathy award.

The New York *Times*, on 23 September 1990, described the increasing popularity of *alternative dispute resolution* (ADR), a new remedy to ease the burden of the contingency fee induced crisis. ADR is illustrated by the case of the 1986 fire at the DuPont Plaza Hotel in Puerto Rico, which was the work of arsonists. One would assume that the arsonists were responsible for the fire, its devastation, and injuries to many people. Surprisingly, more than 100 companies, manufacturers of products ranging from elevators to floor wax, whose flammable products may have helped fuel the blaze, were named as defendants. Most had settled, others were in the final stages of trial after more than 160 days in court at the time of the report. This appears to be a case of deep-pocket justice on a wholesale scale. This example alone is enough to raise many questions. Were all the companies who settled indeed liable, or did at least some of them settle as a reaction to the legal extortion effect of litigation? Do the trial lawyers really want all these companies to remove their products from all hotels?

Trial lawyers argue that the secondary or social aim of their litigation is the reduction of negligence and promotion of safety. I know of only one case when the court made a recommendation, and that was the jury, not the trail lawyers in New York who recommended that qualified emergency physicians should be present in the emergency department at all times.

How Could We Eliminate the CFS?

We could ask the American Bar Association and state bar associations to revise their Code of Ethics declaring the CFS unethical, or we could ask Congress to enact a law prohibiting unearned contingency fees because the CFS is unethical and having an undesirable effect on our justice system and on our economy. This would set us on the right course, but it would take time to return to the common-sense justice just as deep-pocket justice took many years to develop. Lawyers still could represent the poor, who could then pay their fees for services after they receive their compensation as the outcome of settlement or trial.

Because the contingency fee became established as the only system we know of, and because trial lawyers could find alliances in their lobbying effort in groups who perceive that the CFS is beneficial, decisive action by the ABA or Congress is unlikely. If that is the case the constitutionality of the system needs to be examined.

The Contingency Fee System is Probably Unconstitutional

Would the CFS pass the test of constitutionality? Probably not. It has been pointed out by clear thinking people that this system often constitutes extortion from the defendant, who is induced to settle regardless of liability just to save legal costs, and from the plaintiff, who must pay a large portion of the award as a fee, even if it is far beyond the lawyer's usual fee. The system also frequently results in unequal representation because the plaintiff's lawyer, who has financial interest in the outcome of the trial, will provide a more vigorous, more imaginative, and more manipulative representation than the defendant's lawyer who is paid a fixed fee for services regardless of the outcome.[2-3-4]

Is the National Data Bank Fair?

Lastly, to add insult to injury, Congress legislated the establishment of a medical practitioner data bank. A centralized computer will record all adverse actions against health-care professionals including settlement of a suit. Based on this law, how will your lawyer explain to you that to settle does not mean admission of liability, admission of malpractice, professional incompetence, or neglect? Just read the article "National data bank opens to track doctors" that describes a "national system for sharing information about bad doctors." It seems unfair to single out only one group of professionals; it would be less unfair if a national data bank were legislated by Congress for all licensed professionals, applying the same criteria. Lawyers, eg, can represent you negligently, abandon you at will, even misappropriate your money without fear of being listed in such a centralized computer mandated by Congress, with compulsory reporting, compulsory inquiry, and compulsory availability to a plaintiff.

It seems unlikely that Congress will bring up for discussion the corrosive effects of the contingency fee system and we will have to wait with Dr. Snider until "People will cry out loud enough, then and only then will change come and reason, sanity, and justice prevail." Until such time we at least should point out to anyone who is willing to listen that the contingency fee system is the culprit for our litigious society and our deep-pocket system of justice. It is also essential to include the issue of the CFS in the national debate on tort reform.

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Joseph K. Kiraly, M.D., F.A.C.E.P.

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New Executive Director for Fairfield County Medical Association

Mark S. Thompson arrived 1 August to become The Fairfield County Medical Association's new Executive Director. He is replacing Leonard R. Tomat who is retiring after 15 years as FCMA's chief administrator.

Most recently, Mr. Thompson was the Executive Director of the Oneida, Herkimer, Madison, Chenango, and Oswego County Medical Societies in upper New York State. He was also responsible for the daily management of the Central New York Academy of Medicine, the Four County Management Corporation, and the Medical Economics Bureau, a collection agency.

Prior to his affiliations with the five county medical societies, Mr. Thompson served the medical community as a sales representative with Mohawk Hospital Supply in Utica, New York. He was also a purchasing agent at St. Lukes-Memorial Hospital Center in Utica and an assistant administrator of the Benjamin Rush Center in Syracuse. Mr. Thompson held the positions of public health representative for the New York State Department of Health and program consultant for the American Lung Association in Buffalo.

A native of Syracuse, Mr. Thompson received a Bachelor of Science Degree in Administration of Health Services from Ithaca College and attended Chapman College's graduate program in Business Administration.

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October 1941

Meet the Bride and Groom

This year Ohio and Massachusetts have enacted legislation requiring some form of premarital examination and increasing to twenty one the number of states in this category. Because of the striking difference in the recently enacted premarital laws in these two States, a comparison should be of value to the thoughtful physician. Ohio's new law, effective August 18, requires each applicant for a marriage license to furnish a physician's statement, *rendered after an appropriate medical examinati*on,[1] to the effect that such applicant is not infected with syphilis, or, if so infected, is not in a stage of that disease which is communicable or likely to become communicable. Obviously this law is designed primarily to prevent the marriage of a person having syphilis in a communicable stage and in order to meet the requirements of the law more than the taking of a specimen of blood for a standard test for syphilis must be included. It leaves to the physician's own judgment just how thorough or extensive shall be this examination but, as has been found true in other States, the success or failure of this law depends on the thoroughness of the physician consulted by the prospective bride or groom.

Governor Saltonstall of Massachusetts recently signed a premarital examination law passed by that Legislature which leaves nothing to the imagination but requires that a registered practitioner of medicine shall *examine* each of the prospective candidates. Note the wording of the law: "If such physician, in making such examination, discovers evidence of any infectious disease declared by the state department of public health to be dangerous to the public health, he shall inform both parties of the nature of such infectious disease and of the possibilities of transmitting the same to his or her marital partner or to their children. Such examination shall include a standard serological test for syphilis…"[2]

As we have previously remarked,[3] Connecticut congratulates itself on being among the first States to pass a premarital examination law. Our law requires "a statement or statements signed by a licensed physician that each applicant has submitted to a Wasserman or Kahn or other similar standard laboratory test and that, in the opinion of such physician, the person is not infected with syphilis or in a stage of that disease that may become communicable and such statements shall be accompanied by a record of the standard laboratory tests made…[4] Few physicians in this State have read the text of the law, otherwise they would not content themselves with merely taking a specimen of blood for a standard serological test for syphilis.

Some form of an examination is necessary in order to detect the early Wasserman or Kahn negative case of syphilis. What better opportunity to do a thorough job and give the prospective bride or groom the physical examination that should be completed at this time? The unhappiness experienced by newly married couples due to difficulties arising because of ignorance may be prevented by the giving of proper advice at the time of premarital examination. Like the Ohio law, the Connecticut law leaves much to the physician's cooperation and judgment. The law has accomplished much in this State, but should each physician avail himself of his opportunity and make a complete physical examination instead of simply taking a specimen of blood he will be rendering a service to the prospective bride and groom which will reach much beyond the mere eradication of syphilis. This is an age of preventive medicine. The premarital examination carried out in a thorough manner may establish the habit of an annual physical examination and become one of the strongest links in the program of preventive medicine.

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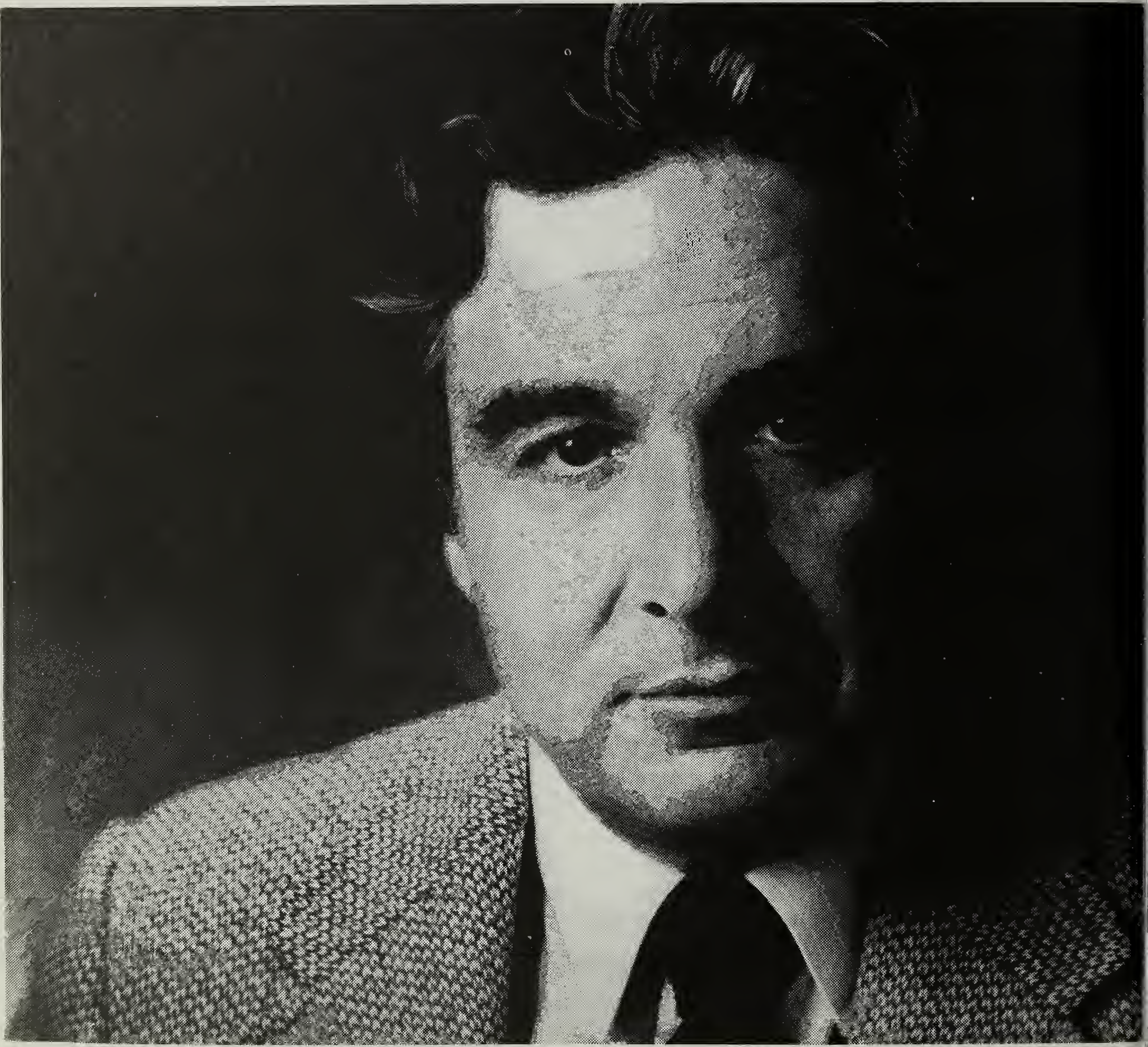
—Editorial from *The Connecticut State Medical Journal*. October 1941.

"I'm accountable to my patients, not to an insurance company. That's just the way I operate."

—Dr. Vincent Catrini, General Surgery, Middletown, CT



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THE PRESIDENT'S PAGE

Physicians and the Providers

America spends 12% of its gross national product on health care. This is nearly three quarters of a trillion, or 750 billion dollars. The question is who controls this money and to whom is it paid.

There are many nonphysician professional and institutional providers in the field of medical care, but we must never forget that most of them are working because the physicians direct and utilize their services. We undoubtedly authorize (but do not receive) approximately 60% of the monies being spent in the health care system, by initiating medical care. Physicians admit patients to hospitals and other facilities, order prescriptions, imaging, laboratory tests, medical equipment, and perform virtually all surgical procedures and initiate most therapies. Unmistakably, if the physician under whose direction most providers work can be controlled, then the majority of the monies being spent on the health care system can also be controlled. Another twenty percent of the money is spent for MD's own fees and overhead, also a target for the cost controllers. The final 20% is for administration of the health care system.

Up to this time the government, the insurance industry, and other brokers of medical care have endeavored to change physicians' habits and to control their instructions to providers of patient care. The major areas of attack have been on length of hospital stay, the use of generic drugs and cheaper treatment modalities. The newest tactic is managed care, which uses the judgment of some physicians to standardize the judgment of many physicians. What effect does this have on a doctor?

Physicians are trained to interview patients, examine them, order appropriate tests and studies, and come up with a diagnosis and treatment plan. Occasionally, the diagnosis is not easily obtained and the physician will ask a trusted and respected colleague for help. If an outsider source such as managed care administration comes along and makes a suggestion, the advice is usually not appreciated. Why? Simply because we have been trained to make clinical decisions, and we do not welcome interference from uninvited administrative sources driven by nonmedical concerns.

Physicians spend four years at college and four years at medical school and then three to five years or more in postgraduate programs. One might think that this would put them all in a very similar economic situation, but this is not the case. Some are salaried and some are fee-for service. Physicians' incomes actually vary widely, from residents' modest stipends in the middle 20 thousands, to the low end of the six-figure range. An entrepreneurial few do even better. There are also other differences within Connecticut, such as the cost of housing, office space, and salaries paid for nurses and secretaries. Differences exist among specialties in the cost of equipment and malpractice insurance. Such differences can breed division. Another factor to consider is the amount of time a physician puts into his medical practice. Some physicians put in twice as much time as others, but may earn only half as much, because of factors of location, specialty, or practice style.

The "Blues" were originally started to pay for big expenses, like in-hospital surgical procedures. Later, commercial insurance companies and government programs like Medicare and Medicaid were built on this original philosophy. The concept of paying more for procedures became deeply rooted in the minds of the medical care brokers. The net effect of this has been to make nonprocedural physicians' work economically second rate. Whether you realize it or not, the physicians of America have been systematically divided by the brokers, ie, government, the insurance industry and big business. As long as physicians can be divided, third-party payers know they will be able to control this expenditure. The university and hospital based physicians compete against community physicians, procedurists against "cognitive" physicians, young against old, and clinic against office-based. If the physicians of America do not close ranks, it will only be a matter of time before the brokers take over. More and more medical budgets are being wrecked by inflation, increased paperwork demands from the brokers, and compliance with ever-changing rules from government agencies.

Mainly, I have focused on physicians as the driving force for health care providers. One must realize that these other individual and institutional providers, too, are trying to keep their bottom lines in black. They too have been divided. It is hospital against hospital, therapist against therapist, and drug company against drug company. As we fight among ourselves, the brokers who control the money are moving in and dictating to us exactly how it will be rationed. Only those groups that will stick together in the face of such divisiveness will have a chance against the forces attacking our economy's beleaguered health care sector.

It is a battle of great armies, and stragglers will not survive.

Anthony P. Redmond, M.D.
President

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ROBERT U. MASSEY, M.D.

MEDICAL articles in the news never fail to make me nervous. They often get their facts wrong, or are misleading, or are ambushes, or at times both true and embarrassing. Last month's headlines, "Hospitals seeking 13% rise in fees," was no exception.[1] Some of the requested increases reported in the Hartford *Courant*, were only 4.6% but others were as high as 42.6%; if comments from medical friends were at all representative, this news both angered and embarrassed. With inflation running at less than 4%, it is hard to explain why a public service needs to increase charges much more than that. Hospitals claim that suppliers are inflating their prices by over 7%, but that it because they know their customers will pay. If these rate increases are representative of those across the country, the percentage of the G.N.P. going to health care, already the highest in the world, will, I estimate, be over 13.5% next year, even if physician fees remain unchanged.

Having justified budgets requests for most of my professional life, I have no doubt that these increases will be justified as well, but surely that is justification by faith, a faith that the public no longer shares. To be sure, our life expectancy has improved and the geriatric crowd is growing, infant mortality is down a little, and AIDS is expensive, but all of that cannot justify higher rates; interest payments are down and salaries are or should be frozen. Business people worry about uncontrollable costs; employee health insurance rates rise as a result of factors they neither understand nor control, forcing them to cut somewhere else to stay in business. During a serious recession that shows few signs of relenting, a tax increase is bad enough; a 13% increase (after a 10.8% increase last year) in hospital rates, 500 million dollars, or over $150 for every man, woman, and child in the state, can only evoke anger and further erode the respect and trust in which these great institutions are held. In the public's mind physicians are part of the same system, a system that seems somewhere and somehow to have lost its sensitivity and its determination to regulate itself.

"If the hospitals won't keep their price increases on a par with those of the rest of the community, the commission must make them,"wrote the *Courant's* editor, adding that maybe we should "consider abolishing the regulators and letting competition and the market place set the price of health care."[2] What market place? Hospitals provide essential services, and sick people with insurance largely paid for by their employers are not hospital shoppers. Even if they have to pay a deductible, they are unlikely to ask the price. Anyway, they are rarely offered a choice.

In medicine the only effective control must come from within, from rigorous self-discipline, and single-minded devotion to service. We must never find ourselves in the position of the banking executive who confessed that his bank collapsed because the regulators failed to do their jobs. Micromanagement by third-party payers surely costs more than it saves, and is an inefficient use of manpower. Yet with cost apparently out of control, it is easy to understand the editorial writer who insists, "The commission must get tougher."

That can be expected to happen unless physicians, and the hospitals whose staffs they comprise, take effective control of both quality and costs, as only they can do. Examples of internal regulation of the profession and of hospitals abound. The Joint Commission on Accreditation of Healthcare Organizations, the Liaison Committee on Medical Education, the National Board of Medical Examiners, the American Board of Medical Specialties—to name but a few—are powerful organs of internal control, signs of a robust conscience at the heart of medicine. There are cynics and revisionists who see in these institutions of quality control only self-interest, but those of us who have worked with them or seen them in action know better. At the least they represent enlightened self-interest.

Optimists may take heart when they see a 13% increase in hospital rates and an even steeper rise in Medigap rates: the worse things get the sooner we'll fix them. Unfortunately the fixers are not experts in health policy matters, but rather politicians goaded by an angry public to do things that will almost certainly make the whole thing worse. To let such important matters slip through our hands is the height of folly, and it will be folly compounded to sit on the back benches carping at our political masters as they try vainly to solve problems they barely understand.

ROBERT U. MASSEY, M.D., Professor, Division of Humanistic Studies in Medicine, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

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LAW, MEDICINE, AND PUBLIC POLICY

Medical Malpractice 1991: Uncovering Useful Data

JOSEPH M. HEALEY, J.D.

DISCUSSIONS of the strengths and weaknesses of the medical malpractice system in the United States have been hindered by the emotionally charged environment in which the discussions have occurred and by the absence of good research data about the system. For many participants, whether doctors, lawyers, insurers, or patients, the malpractice system is an unpleasant experience, inspiring anger and frustration. As a result many comments and analyses of the system reflect the disappointment of the participants, rather than an impartial consideration of the system's strengths and weaknesses. Data about malpractice have been difficult to obtain and, when available, often have been of limited value.

Recognizing the need for useful data, in 1985 the Robert Wood Johnson Foundation established a program to examine the concept of negligent medical care and to evaluate the effectiveness of reforms and the existing system. Nineteen projects were funded. The results are now beginning to emerge. The Foundation has published a summary discussion of the more interesting projects and findings.[1] One of the projects has published three widely publicized articles in the *New England Journal of Medicine*.[2] Two special issues of *Law and Contemporary Problems*, joined together under the title, "Medical Malpractice: Lessons for Reform," have been devoted to recent malpractice research, including several of the Foundation's projects.[3] This research and these data represent an important step in an attempt to shift the focus of policy discussion from emotional experience to empirical data and to provide an opportunity to reexamine this most divisive issue in the law-medicine relationship.

The first of the major themes emerging from the projects should come as no surprise to those involved in malpractice: "The tort and insurance liability systems as they are now structured, provide neither an efficient nor an equitable means of compensation for injured parties nor adequate deterrence against medical negligence."[1(p1)]

Several of the projects addressed this theme. The Harvard Medical Practice Study had four major goals: (1) to determine the rate and pattern of medical injury and negligent medical injury in hospitals; (2) to match incidents of medical injury with specific claims behavior; (3) to estimate the economic costs associated with medical injuries; and (4) to determine if malpractice litigation has a deterrent effect on negligence.[1(p6)] Addressing these objectives would in turn contribute to an understanding of the extent to which the current system achieves all or some of its goals.

The Harvard Study researchers reviewed over 30,000 randomly selected hospital records from 51 randomly selected acute care, nonpsychiatric hospitals in New York state. The study group identified 1,278 adverse events ("a medical injury caused by medical practice, as opposed to a disease process, which leads to a prolongation of a hospitalization or a disability at the time of discharge") and 306 negligent adverse events ("an adverse event associated with substandard medical care"). This represented an adverse event rate of 3.7% and a negligent adverse event rate of 1%. The percentage of adverse events due to negligence was 27.6%. Using these data, the researchers estimated that the 2,631,863 hospital discharges involved 98,609 patients who suffered adverse events and 27,179 patients who suffered negligent adverse events.

Using a variety of estimation techniques, the researchers concluded that approximately 3,000 to 4,000 malpractice claims are filed each year. This represents approximately one claim for every 7 to 9 negligent adverse events. Further examination of the claims filed revealed that a substantial number of claims without a compensable injury or a breach of duty, requirements for a successful malpractice suit, had been held. In fact, the ratio of filed claims to negligent adverse events is more like 1 to 50.

There are two consequences of these findings. First, there are many negligent adverse events for which recovery should be available under our present system in which there is no recovery. The current system does not meet its goal of compensating those who have been injured through the negligence of a health professional. Second, there are many adverse events for which recovery is not possible under the existing fault-based system, but recovery would be possible under a "no-fault" system. The substitution of no-fault as a replacement for the existing system would be less attractive, if the larger number of eligible claims threatened any cost savings by changing to no-fault.

Discussion will continue in next month's column.

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JOSEPH M. HEALEY, J.D., Professor, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

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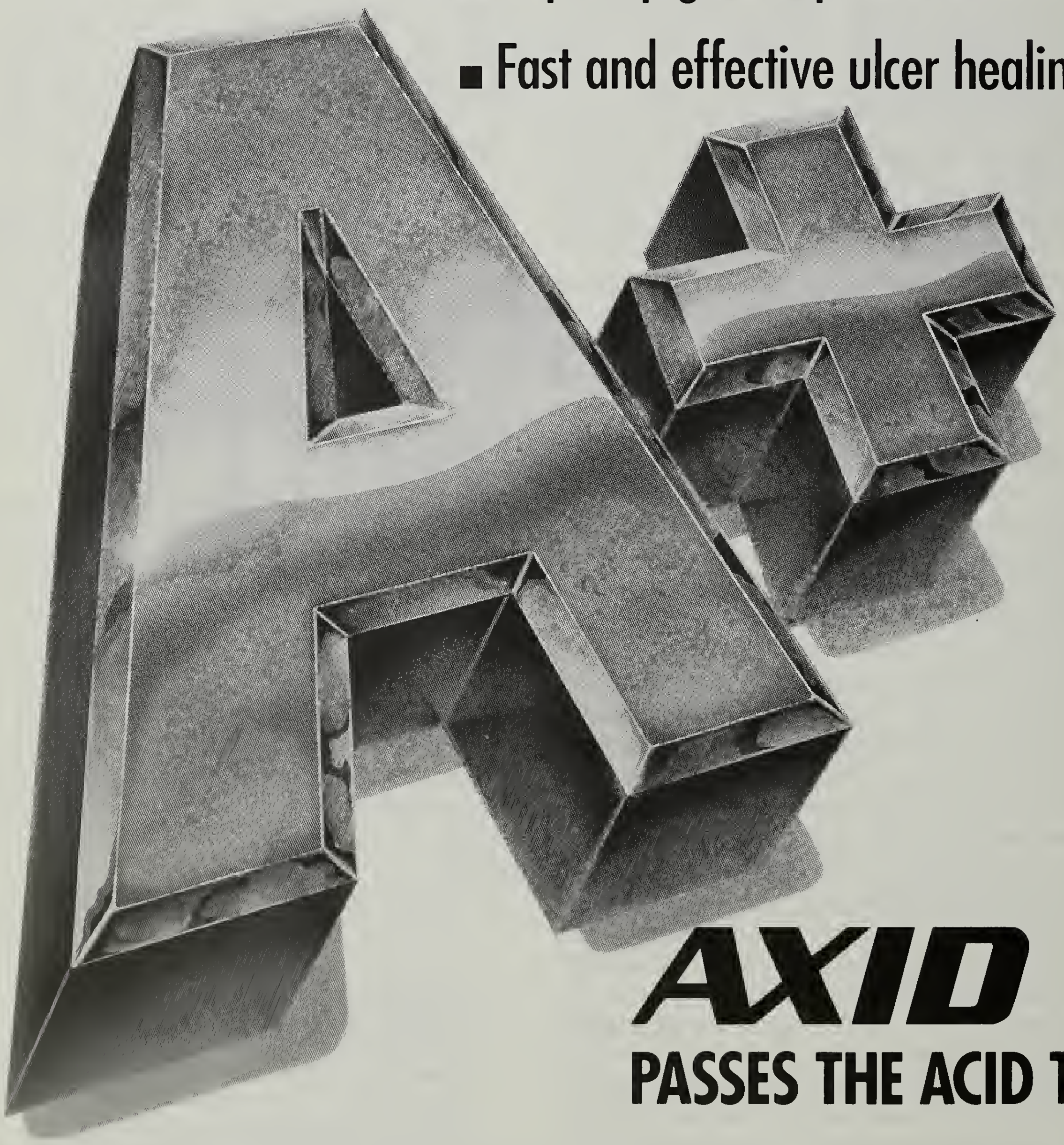

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Carcinogenesis, Mutagenesis, Impairment of Fertility—A 2-year oral carcinogenicity study in rats with doses as high as 500 mg/kg/day (about 80 times the recommended daily therapeutic dose) showed no evidence of a carcinogenic effect. There was a dose-related increase in the density of enterochromaffin-like (ECL) cells in the gastric oxyntic mucosa. In a 2-year study in mice, there was no evidence of a carcinogenic effect in male mice, although hyperplastic nodules of the liver were increased in the high-dose males as compared with placebo. Female mice given the high dose of Axid (2,000 mg/kg/day, about 330 times the human dose) showed marginally statistically significant increases in hepatic carcinoma and hepatic nodular hyperplasia with no numerical increase seen in any of the other dose groups. The rate of hepatic carcinoma in the high-dose animals was within the historical control limits seen for the strain of mice used. The female mice were given a dose larger than the maximum tolerated dose, as indicated by excessive (30%) weight decrement as compared with concurrent controls and evidence of mild liver injury (transaminase elevations). The occurrence of a marginal finding at high dose only in animals given an excessive and somewhat hepatotoxic dose, with no evidence of a carcinogenic effect in rats, male mice, and female mice (given up to 360 mg/kg/day, about 60 times the human dose), and a negative mutagenicity battery are not considered evidence of a carcinogenic potential for Axid.

Axid was not mutagenic in a battery of tests performed to evaluate its potential genetic toxicity, including bacterial mutation tests, unscheduled DNA synthesis, sister chromatid exchange, mouse lymphoma assay, chromosome aberration tests, and a micronucleus test.

In a 2-generation, perinatal and postnatal fertility study in rats, doses of nizatidine up to 650 mg/kg/day produced no adverse effects on the reproductive performance of parental animals or their progeny.

Pregnancy—Teratogenic Effects—Pregnancy Category C—Oral reproduction studies in rats at doses up to 300 times the human dose and in Dutch Belted rabbits at doses up to 55 times the human dose revealed no evidence of impaired fertility or teratogenic effect; but, at a dose equivalent to 300 times the human dose, treated rabbits had abortions, decreased number of live fetuses, and depressed fetal weights. On intravenous administration to pregnant New Zealand White rabbits, nizatidine at 20 mg/kg produced cardiac enlargement, coarctation of the aortic arch, and cutaneous edema in 1 fetus, and at 50 mg/kg, it produced ventricular anomaly, distended abdomen, spina bifida, hydrocephaly, and enlarged heart in 1 fetus. There are, however, no adequate and well-controlled studies in pregnant women. It is also not known whether nizatidine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nizatidine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers—Studies in lactating women have shown that 0.1% of an oral dose is secreted in human milk in proportion to plasma concentrations. Because of growth depression in pups reared by treated lactating rats, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

Pediatric Use—Safety and effectiveness in children have not been established.

Use in Elderly Patients—Healing rates in elderly patients were similar to those in younger age groups as were the rates of adverse events and laboratory test abnormalities. Age alone may not be an important factor in the disposition of nizatidine. Elderly patients may have reduced renal function.

Adverse Reactions: Clinical trials of varying durations included almost 5,000 patients. Among the more common adverse events in domestic placebo-controlled trials of over 1,900 nizatidine patients and over 1,300 on placebo, sweating (1% vs 0.2%), urticaria (0.5% vs <0.01%), and somnolence (2.4% vs 1.3%) were significantly more common with nizatidine. It was not possible to determine whether a variety of less common events were due to the drug.

Hepatic—Hepatocellular injury (elevated liver enzyme tests or alkaline phosphatase) possibly or probably related to nizatidine occurred in some patients. In some cases, there was marked elevation (>500 IU/L) in SGOT or SGPT and, in a single instance, SGPT was >2,000 IU/L. The incidence of elevated liver enzymes overall and elevations of up to 3 times the upper limit of normal, however, did not significantly differ from that in placebo patients. All abnormalities were reversible after discontinuation of Axid. Since market introduction, hepatitis and jaundice have been reported. Rare cases of cholestatic or mixed hepatocellular and cholestatic injury with jaundice have been reported with reversal of the abnormalities after discontinuation of Axid.

Cardiovascular—In clinical pharmacology studies, short episodes of asymptomatic ventricular tachycardia occurred in 2 individuals administered Axid and in 3 untreated subjects.

CNS—Rare cases of reversible mental confusion have been reported.

Endocrine—Clinical pharmacology studies and controlled clinical trials showed no evidence of antiandrogenic activity due to nizatidine. Impotence and decreased libido were reported with equal frequency by patients on nizatidine and those on placebo. Gynecomastia has been reported rarely.

Hematologic—Fatal thrombocytopenia was reported in a patient treated with nizatidine and another H_2-receptor antagonist. This patient had previously experienced thrombocytopenia while taking other drugs. Rare cases of thrombocytopenic purpura have been reported.

Integumental—Sweating and urticaria were reported significantly more frequently in nizatidine- than in placebo-treated patients. Rash and exfoliative dermatitis were also reported.

Hypersensitivity—As with other H_2-receptor antagonists, rare cases of anaphylaxis following nizatidine administration have been reported. Rare episodes of hypersensitivity reactions (eg, bronchospasm, laryngeal edema, rash, and eosinophilia) have been reported.

Other—Hyperuricemia unassociated with gout or nephrolithiasis was reported. Eosinophilia, fever, and nausea related to nizatidine have been reported.

Overdosage: Overdoses of Axid have been reported rarely. If overdosage occurs, activated charcoal, emesis, or lavage should be considered along with clinical monitoring and supportive therapy. Renal dialysis does not substantially increase clearance of nizatidine due to its large volume of distribution.

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Letter to the Editor

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COOLING OFF AFTER EXERCISE

To the Editor: It seems important for fitness buffs to pay attention to "warm-up" and "cool-off" in their exercise routines, especially the cool-down. You can't just stand around after a strenuous workout, — disaster has followed. People are more comfortable when the changes in homeostasis are gradual and usually take precautions, but when the subject has forgotten to keep moving it may be different!

The common cause of heart attacks is stress with coronary artery disease. Plaques may form at an early age with lipid overload, and attacks later in life are triggered by ischemia and anoxemia. The complex physiology of organ blood supply (called "hematometakinesia" by de Bakey) involves heart-rate, regional blood vessel constriction and dilatation, and neurogenic coordination of sensory information.

A rapid blood stream has momentum, and a sudden drop in "demand" could produce the crowding of "supply" and overload somewhere in the vascular bed. The subject is usually warned about this by physical discomfort, but distractions may cause individuals to pay no attention.

The cardiac cart is pulled by a team, the ventricular pair, and they have to be "in sync." The constant reminder to "cool off slowly" must always be in play; collapse has occurred from mere immobility after running hard; this is where the precaution ought to be kept in mind.

Sidney Vernon, M.D.

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Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalmic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon® is indicated as a sympathicolytic and mydriatric. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

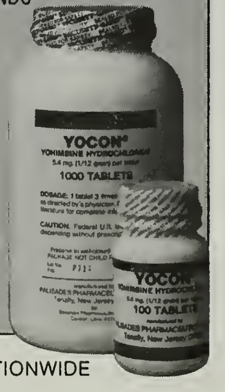
Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.[1,2] Also dizziness, headache, skin flushing reported when used orally.[1,3]

Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.[1,3,4] 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to ½ tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.[3]

How Supplied: Oral tablets of Yocon® 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:
1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

Rev. 1/85



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Robert U. Massey, M.D., 160 St. Ronan Street, New Haven, CT 06511

Managing Editor *(Name and Complete Mailing Address)*
Wanda E. Jacques, 160 St. Ronan Street, New Haven, CT 06511

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Full Name	Complete Mailing Address
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(1) ☒ Has Not Changed During Preceding 12 Months
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(Signature) Robert U Massey
Robert U. Massey, M.D., Editor

PS Form 3526, Feb. 1989

The Month's Reading in Review

TIMOTHY B. NORBECK

- All eyes are on Initiative 553 to come before Washington voters this November...The Washington measure would limit the governor and lieutenant governor to two terms; state legislators to 10 consecutive years (or three terms in the House and two in the Senate) and members of Congress to 12 consecutive years (two terms in the case of U.S. Senators)...Because Initiative 553 would allow incumbents to serve only one more term after the measure is approved, one of the victims would be U.S. House Speaker Thomas S. Foley...Foley and Governor Booth Gardner were among those who unsuccessfully challenged the measure by asking the Washington Supreme Court to keep it off the ballot in November on the grounds that it was unconstitutional.
- The AMA reports that the percentage of physicians with direct financial contracts with hospitals dropped substantially during the 1980s...In 1990, 19 percent of all physicians had a written or verbal contract under which a hospital paid them directly - down from 26 percent in 1981...In both years, pathologists had the highest percentage (78 percent in 1981 and 60 percent in 1990)...Obstetrics-gynecology had the lowest percentage (10 percent in 1981 and 7 percent in 1990)...Pediatrics was the only specialty in which the percentage grew (17 percent in 1981 and 21 percent in 1990).
- In 1990, Medicare accounted for 16 percent of total national health expenditures...Those expenditures are estimated to have represented 2 percent of the 1990 GNP...Of all health insurers, Medicare was the single largest purchaser of hospital and physician care in 1989, purchasing approximately 40 percent of hospital care and 20 percent of physician care.
- A study by Health Care Investment Analysts reports that about 18 percent of all U.S. hospitals have suffered "sufficient declines in occupancy, profitability and liquidity to be labeled distressed"...The survey indicates that 1,059 hospitals were distressed by the end of the 1991 second quarter - up from 538 from the same period a year ago.
- With respect to the law, the *Wall Street Journal* claimed that "With a series of perverse incentives toward lawsuits, we alone in the world turned the tort liability system into a whole parasitic industry"...The *Journal* also referred to a report which indicated that "foreign manufacturers can have product liability rates as little as 2 percent of the rates U.S. manufacturers must pay."
- David Gergen of *U.S. News & World Report* wrote that "The law once was one of the nation's most honorable professions...Over the past quarter century, however, courts have rewritten the rules so that a lawsuit is no longer an option of last resort but a weapon of choice, a reach for the jackpot"...He goes on to say that it is a "stunning commentary that America has 5 percent of the world's population but 70 percent of the lawyers but clearly we need to delawyer our society."
- Calling Canada's ban on tobacco advertising "social engineering" and "state moralism", Quebec Superior Court Justice Jean-Jude Chabot ruled that the three-year-old law is unconstitutional because it violates the right to free speech...Tobacco companies and anti-smoking groups acknowledged that it was the first known successful legal challenge of such a ban...According to the *Wall Street Journal*, Judge Chabot claimed that "There isn't any proof that advertising itself is a danger to public health"...As Aristotle said, the word 'dog' never bit anyone.
- This past month, a federal judge heard the first challenge to Louisana's new law setting prison terms

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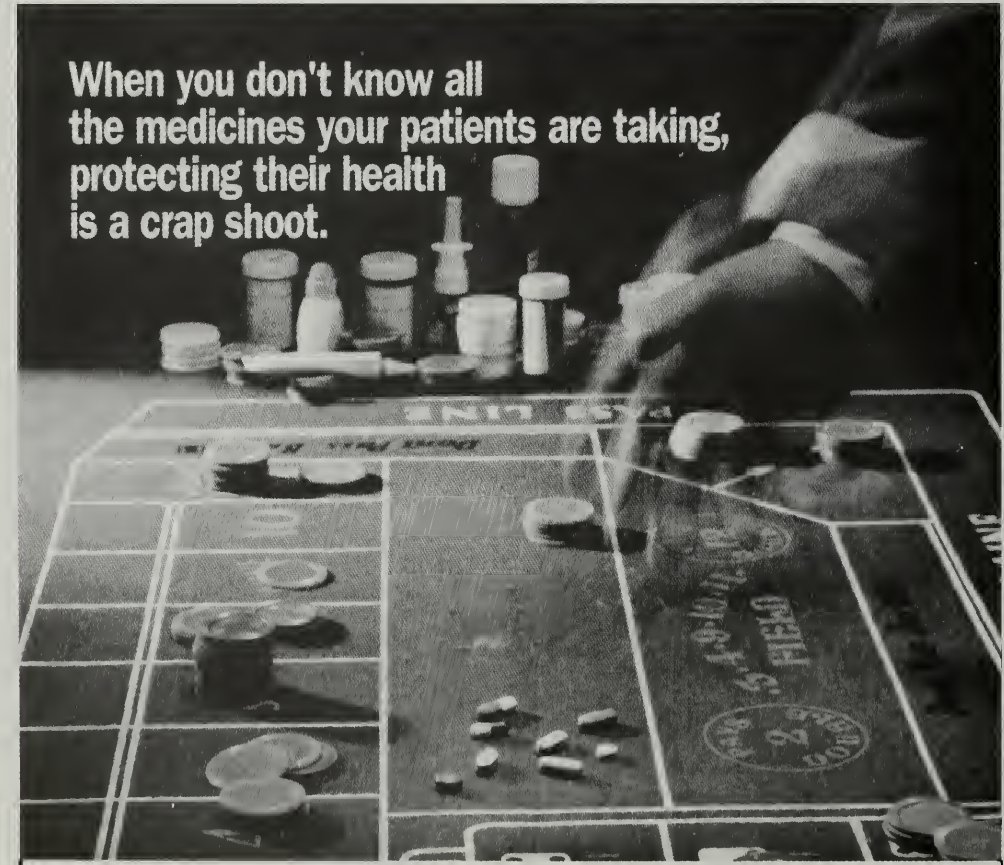
TIMOTHY B. NORBECK, Executive Director of the Connecticut State Medical Society.

of up to 10 years for physicians who perform abortions...The case is likely to reach the U.S. Supreme Court.

- Despite concern over the deficit, a $150,000 grant has been made available in the current federal budget to study the legendary feud between William Hatfield and Randolph McCoy...Porkbusters, the name for a large coalition of taxpayers groups and some congressional representatives, calls the Hatfield - McCoy program one of the silliest studies ever...Other pork-barrel programs include $320,000 to purchase the house of President William McKinley's mother-in-law and $1.7 million for a preliminary survey for converting Biscayne Boulevard in downtown Miami into "an exotic garden."
- U.S. Senator Robert C. Byrd (D, West VA) is making good on his pledge to be a personal "billion dollar industry"...Just two years after being named chairman of the Senate Appropriations Committee, he has steered more than $750 million worth of Federal projects and agencies (and more than 3,000 Federal jobs) out of Washington and into his state...The FBI's new $185 million fingerprint center will soon be built in Clarksburg, bringing in 2,600 new jobs...Now Senator Byrd is targeting the CIA and hopes to move 3,000 of its jobs to West Virginia.



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From the Executive Director's Office

CALL

SEMI-ANNUAL MEETING OF THE HOUSE OF DELEGATES

The 1991 Semi-Annual Meeting of the House of Delegates will be held at the Ramada Inn, 275 Research Parkway, Meriden. The meeting will commence at 12:30 p.m. on Thursday, November 21, and will continue until all business has been concluded.

11:30 Registration
12:20 Call to Order

Anthony P. Redmond, M.D., President
Theodore Zanker, M.D., Speaker of the House
Marjorie G. Petro, M.D., Secretary

INTRODUCTION OF RESOLUTIONS

Article V, Section 12, Par. 3 of the Bylaws of the Society provides that:

Resolutions may be introduced by any Active, Life Member, Student Member or Postgraduate Physician Member of The Society, in compliance with the following provisions.

a. All resolutions, reports and similar items of business submitted in writing and received at the office of the Executive Director not later than thirty days before the date scheduled for that meeting shall be considered as regular business of the House of Delegates.

b. Component county associations or the Student Member or Postgraduate Physician Member Associations whose meetings are held later than thirty-five days prior to the date of the House of Delegates shall be allowed five days after the close of such meeting in which to submit resolutions, reports and similar items of business to the Executive Director's office and still have such material considered as regular business. In no event, however, may such resolutions, etc., be considered regular business if they are received later than fifteen days prior to the date of the meeting.

c. Reports, recommendations, resolutions or other new business may be presented to the House of Delegates by the Council of The Society at any time and shall be considered as regular business.

d. Any business which does not qualify as regular business in accordance with the foregoing provisions may be accepted for consideration by a majority vote of the delegates present and shall be referred at once by the Speaker to a reference committee. When business is introduced under the provisions of this paragraph the vote shall be taken without debate, except that the introducer shall be allowed not more than two minutes to explain why it should be considered as regular business.

PROPOSED AMENDMENTS TO THE BYLAWS

The following proposed amendments to the Bylaws were presented to the House of Delegates on May 8, 1991 and were tabled for consideration and action at the next regular meeting of the House of Delegates.

In accordance with the Bylaws, these amendments are being published in *Connecticut Medicine* "on one or more occasions prior to the next meeting—at which meeting the amendments shall be taken off the table and acted upon by the House of Delegates.

SUBJECT: SCIENTIFIC PROGRAM AND SECTION MEETINGS

PURPOSE: TO REMOVE DESIGNATED TIME FOR THE SCIENTIFIC PROGRAM AND SECTION MEETINGS

The Council recommends the following changes:

(DELETIONS IN BRACKETS AND CAPITALS - NEW MATERIAL UNDERLINED)

ARTICLE V, Section 1, Powers and Duties

The House of Delegates may provide for (A DIVISION OF THE SCIENTIFIC ASSEMBLY OF THE SOCIETY INTO) sections for the presentation and discussion of subjects pertaining to the science and art of medicine.........

ARTICLE V, HOUSE OF DELEGATES, Section 7, Regular Meetings

The House of Delegates shall meet annually (DURING THE WEEK OF THE SCIENTIFIC ASSEMBLY OF THE SOCIETY) at a time and place designated by the Council.

ARTICLE VIII-(SCIENTIFIC ASSEMBLY) *CSMS SPECIALTY SECTIONS*

ARTICLE VIII, (SECTION 1, DEFINITION)

(THE SCIENTIFIC ASSEMBLY OF THE SOCIETY IS

THE CONVOCATION OF ITS MEMBERS FOR THE PRESENTATION AND DISCUSSION OF SUBJECTS PERTAINING TO THE SCIENCE AND ART OF MEDICINE).

ARTICLE VIII, (SECTION 2, MEETINGS, PAR 1)

(Par. 1. GENERAL MEETINGS OF THE SOCIETY SHALL BE HELD ANNUALLY, AT A TIME AND PLACE DESIGNATED BY THE COUNCIL. THE ANNUAL MEETING OF THE HOUSE OF DELEGATES SHALL BE HELD DURING THE WEEK OF THE SCIENTIFIC ASSEMBLY.)

ARTICLE VIII, *Section 1, SPECIALTY SECTIONS*

(PAR 2, SECTIONS) is changed to *Par 1. Sections.*

Par. a, Purposes: To conduct (THE WORK OF THE SCIENTIFIC ASSEMBLY) *Medical Specialty Activities, Continuing Medical Education* and for related purposes, the formation of Sections of the (SCIENTIFIC ASSEMBLY) Society may be authorized by the House of Delegates.

Par. b, Authorization: *Specialty* Sections of the *Society* (SCIENTIFIC ASSEMBLY) may be created or discontinued by the House of Delegates.........

Par. d, Membership: It is the intention of the House of Delegates that the sole qualifications for physician membership in a Section (OF THE SCIENTIFIC ASSEMBLY) shall be.........

Par. f, Meetings: Each Active Section shall hold an annual meeting. (DURING THE ANNUAL MEETING OF THE SCIENTIFIC ASSEMBLY OF THE SOCIETY, OR, IF NOT PRACTICAL DUE TO A CONFLICT WITH A MEETING OF A RECOGNIZED NATIONAL ORGANIZATION, DURING THE SAME CALENDAR MONTH AS THE SCIENTIFIC ASSEMBLY AND AT SUCH OTHER TIMES AS THE MEMBER OR OFFICERS MAY DEEM ADVISABLE.) The officers of each Active Section shall arrange the programs for the annual meeting (DURING THE SCIENTIFIC ASSEMBLY) in accordance with rules established by the Council and the House of Delegates.

Par. g, Definition of Active Section. With reference to preceeding Subparagraphs e and f, and Active Section of the (SCIENTIFIC ASSEMBLY OF) Society is defined as one that complies fully with the provisions of these subparagraphs annually. Failure to hold a meeting of the Section (DURING THE SCIENTIFIC ASSEMBLY) for three consecutive years shall be cause for the Section to lose automatically its active status, and, further, shall be considered cause for the House of Delegates to withdraw authorization for the Section.

ARTICLE VIII, SCIENTIFIC ASSEMBLY, Section 3 (REGISTRANTS) *SECTION MEETINGS*

(DELETE ENTIRE PAR. 1)

RENUMBER PAR. 2 AS SECTION 3

ARTICLE VIII, SCIENTIFIC ASSEMBLY, Section 4. Quorum

A quorum at any (GENERAL MEETING OR) Section meeting (OF THE SCIENTIFIC ASSEMBLY) shall be (THOSE PRESENT AT A DULY CALLED MEETING, OR IN THE CASE OF A Section), the number of proportion designated by the Section.

DELETE ANY OTHER REFERENCE TO SCIENTIFIC ASSEMBLY THAT APPEARS IN THE BYLAWS.

COUNCIL MINUTES

Thursday, September 19,1991

ATTENDANCE

Present in addition to the Chairman, Dr. Joseph C. Czarsty, were Drs. Beck, Blue, Cottle, Deren, Eslami, M. Fox, Franklin, Freedman, Hollister, Kamens, McDonnell, Meridy, Orphanos, Parke, Petrie, Petro, Redmond, Sadowski, Sosa, Wetstone, Zanker, Zeppieri.

Also present were: Mr. Norbeck, Mrs. Lindquist, Mr. Brunell, Ms. Ballou, Mr. Garofalo, Mrs. Connelly, Mr. Thompson (FCMA), Mr. Coffey (HCMA), Ms. Harney (NHCMA).

Absent were: Drs. Ahamed, Blake, Bobruff, Brooks, Dardick, B. Fox, Hosking, Keating, Lesnik, Parikh, Tesoro, Van Nostrand, Wolfson.

Report of Related Organization

CPRO: At the last meeting of the AMA House of Delegates, CSMS submitted the name of Edward Kamens, M.D. in nomination to participate on the National Uniform Clinical Data Set (UCDS) Advisory Panel. His nomination was accepted by the AMA and he was asked to serve together with representatives of the Practice Parameters Partnership and the Practice Parameters Forum on this panel designed to develop a strategy for review and refinement by physician organizations of this computer based data collection system. As Medical Director of the CPRO, one of two in the country that conducted the pilot study of this system, he is uniquely suited for assuring accuracy and conformity of the UCDS case review screens and professionally developed parameters of care. Dr. Kamens gave a report on the meeting of the panel which was held in Baltimore on August 21 and stated that it was a fruitful meeting. It is expected that additional meetings will be held. He also reported that he was requested by the AMA to go to Washington and give testimony for the AMA Task Force on the PROs and the role of the PRO in Connecticut. In addition, he has been invited to Chicago to address the medical directors of the insurance companies that handle Part B of Medicare on the role of medical directors of peer review organizations. With initiation of the UCDS program, the computerized program, there is need for CPRO to recruit more physician advisors. Dr. Kamens reported that of particular interest now is that the preadmission certification will be discontinued after October 1.

Report of the President

Bylaw Amendment Re House of Delegates: Dr. Redmond presented a bylaw amendment which would make it not mandatory to have a semi-annual meeting of the House of Delegates. Following discussion, it was VOTED to present the proposed bylaw amendment to the House of Delegates.

CSMS Strategic Planning: Dr. Redmond reported that discussions with colleagues and physicians over the past few years led him to believe that the time had come for CSMS to develop a strategic plan to address the future needs of the Society and its members. Issues such as membership retention and recruitment (with an emphasis toward the recruitment of young, minority and women physicians), legislative goals, involvement with the Council of New England State Medical Societies, generating non-dues income, preserving and strengthening the Auxiliary, defining public affairs objectives, more coalition building, and refining and prioritizing existing programs. He recommended that a retreat be held involving, the CSMS officers, all past presidents, members of the Council and the Committee on Statewide Medical Planning. It was VOTED to have a retreat. Dr. Redmond was requested to appoint a committee to make preliminary plans as to date and financing.

Report of the Executive Director

RBRVS: Mr. Norbeck provided the members of the Council with a copy of a Fax received from the AMA indicating that HCFA backed down on everything except the behavioral offset. He commented that Gail Wilensky remains intransigent of that portion of the reduction in the conversion factor, so that only ten percent of the sixteen percent we sought would be cut. The AMA intends now to carry the fight to the Congress in the form of legislation and is now formally supporting the Stark bill. AMA is now asking for CSMS to obtain sponsors for the Stark bill and having Senator Rockefeller introduce a companion bill. It was reported that getting the full Connecticut congressional delegation signed up would not be a problem.

Mr. Norbeck reported that there was an error in the AM News coverage in August which listed twenty states where physicians made RBRVS congressional visits and did not list Connecticut among the twenty. The editor of AM News was called and informed that Connecticut was one of the first to get letters out to its membership and met with almost all of the congressional delegation. AM News offered CSMS an opportunity to place a letter to the editor in the publication. A copy of the letter which will be submitted from Dr. Redmond to AM News was distributed to members of the Council. It was suggested that a copy of the letter should be sent to the President of the AMA.

Health Care Expo: At the August 14 Council meeting Mr. Norbeck had mentioned a letter received from Dennis May of the Connecticut Hospital Association regarding their Health Care Expo (formerly run by HCMA) in April of 1992 inviting CSMS to participate in developing an educational program specifically for physicians during the 1992 Expo. At the time, it was voted that staff discuss this project with HCMA before any action was taken. It discussing the program with the Executive Director of HCMA, it was learned that although there were some problems with the organizers, he saw no reason why CSMS should not participate in the program.

CSMS Charitable Trust: He reported that CSMS received a very appreciative letter from the Salvation Army pertaining to the Charitable Trust Donation made to them during the annual meeting of the House of Delegates in May. It was also noted that CSMS donation was mentioned prominently in their Southern N.E. Newsletter, "Yankee Clippings" and their Eastern Territorial Newspaper, "The Good News" which goes all over the northeast into Pennsylvania and Ohio.

Report of the Auxiliary

Mrs. Joseph Czarsty was unable to attend the meeting, but submitted a written report. The report mentioned that the Auxiliary is still very weak, with the exception of Middlesex County, which is the only real active group. Apparently, other states are having difficulty and Vermont, Maine, and New Hampshire are only partially surviving. The southern and western states have great enthusiasm which was noted first hand by attendance at the Arkansas annual meeting.

It was noted that with the Bicentennial Year it is a great opportunity to involve members of the Auxiliary, not only with the ball but other events. They are ready and willing to assist in anyway possible.

Mrs.Czarsty stated that they need the Council's help to promote the Auxiliary and their activities and this should be done at county level also. She noted, that in order for the Auxiliary to survive, CSMS should include them in their activities and promote Auxiliary membership.

Nominations for Council of the AMA

A list of members of the AMA Councils for which AMA is soliciting nominees to fill vacancies that will occur in 1992 was distributed with the agenda to all members of the Council. Dr. Czarsty reported that in the previous action of the Council Dr. Petrie had been nominated for appointment to the AMPAC Board and Dr. Freedman was nominated for appointment to the Committee on Legislation. No other nominations were made.

CMMI

Resignation from Board: It was VOTED to accept, with regret, the resignation of Jerome K. Freedman, M.D. from the Board of Connecticut Medical Management, Inc. Dr. Freedman submitted his resignation due to other heavy commitments.

Physician Negotiation with Third Party Payer

Jerome Freedman, M.D. submitted a written report on AMA activities concerning ways and means to improve physicians and medical societies ability to negotiate with third party payers. It was VOTED to receive the report as information.

Nomination of CPRO Directors

It was VOTED to confirm the renomination of Kenneth Dardick, M.D. and Earle Sittambalam, M.D. to CPRO for election to the Board of Directors.

Reorganization of Meetings of the House of Delegates

Theodore Zanker, M.D. submitted suggestions as to various changes that could be made in the structure of meetings of the House of Delegates and CSMS. It was VOTED that Dr. Zanker's suggestion become part of the agenda for the retreat which was discussed in the President's report.

It was suggested that appropriate posters, etc. be displayed at CSMS meetings outlining the accomplishments of CSMS, such as the development of CPRO, CMIC, M.D. Health Plan, Workers' Compensation Symposiums and legislation achievements.

Recommendations of Ad Hoc Committee on HIV Testing

The Council reviewed a reworded version of a recommendation concerning "Occupational HIV-Infection and Disability" that was submitted to the Council at its last meeting and which had been returned to the committee for clarification. Also included in the report was a recommendation that CSMS endorse and sponsor the AMA's new HIV-Indemnity Policy. After prolonged discussion, it was VOTED to table the report and refer it back to the committee for further clarification.

Peer Review

Jerome Freedman M.D. submitted a letter accompanied by a report of the AMA Board of Trustees listing recommendations concerning litigation over hospital peer review decisions. He reported that there is a new concept called the "state exemption." The state must have a clear, positively stated policy on peer review and must actively supervise peer review matters of medical societies, hospitals or wherever they occur. If the state does this, there would be no suit against the physicians doing peer review, because the reviewer would have the right of appeal from decisions made by a medical society or by a hospital peer review committee to a state body which has the power to hear medical and non-medical matters and to overturn decisions. It was VOTED that the letter and report and recommendations of the AMA be referred to a committee, to be appointed by the Chairman of the Council, that should meet with the State Commissioner of Health to determine whether there is need for any action to be taken by the Medical Society and the State of Connecticut.

N.B.:*The foregoing is a summary of the proceedings and actions of the Council on Thursday, September 19, 1991. Detailed minutes of the meeting are on file at 160 St. Ronan Street, New Haven, for perusal by any interested members of the Society.*

IN MEMORIAM

GUARDINO, JOSEPH J., SR., Univ. of Vermont, 1962. Doctor Guardino was a family practitioner in Manchester from 1963 through 1989. He was a member of the Hartford County Medical Association and the Connecticut State Medical Society. Died August 7, 1991.

KIM, PETER C., National University Taiwan, 1965. Doctor Kim was an anesthesiologist with the Stamford Anesthesiology Associates. Doctor Kim was a member of the Fairfield County Medical Association, Connecticut State Medical Society and the American Medical Association. Died July 18, 1991.

KIRSCH, NEVILLE, Long Island College of Medicine, 1940. Doctor Kirsch was a dermatologist, taught at Yale University and was a Consultant for the Community Health Care Plan. Doctor Kirsch was a member of the Hartford County Medical Association and the Connecticut State Medical Society. Died July 18, 1991.

MACDOUGALL, ARCHIBALD D., Cornell University, 1943. Doctor MacDougall was the retired director of medicine at Electric Boat in Groton, CT. Doctor MacDougall was a member of the New London County Medical Association, Connecticut State Medical Society and the American Medical Association. Died June 23, 1991.

MILLER, ROBERT B., Loyola University College of Medicine, 1942. Doctor Miller was a psychiatrist and retired superintendent of Fairfield Hills Hospital. Doctor Miller was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Died July 9, 1991.

ORTH, ROBERT H., Cornell University, 1953. Doctor Orth was an orthopedic in Stamford since 1961. He had retired to Warren, Vermont and was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Died July 19, 1991.

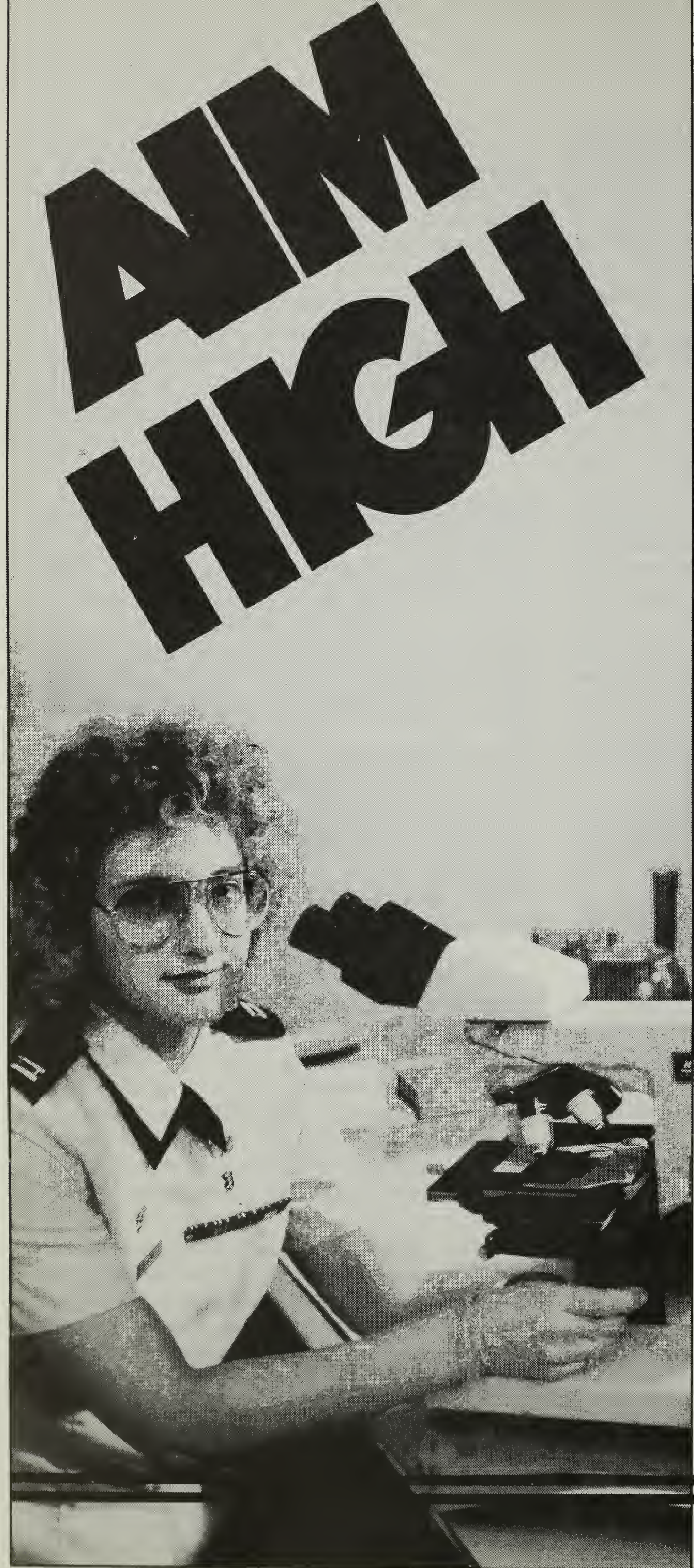
RASMUSSEN, HANS N., Tufts Medical School, 1925. Doctor Rasmussen was a general practitioner in Montville from 1929 until his retirement in 1986. Doctor Rasmussen was a member of the New London County Medical Association, Connecticut State Medical Society and the American Medical Association. Died July 6, 1991.

SCHNAP, ISADORE, Long Island College Medical School, 1929. Doctor Schnap was a psychiatrist in Hartford and was a member of the Hartford County Medical Association, and the Connecticut State Medical Society. Died August 11, 1991.

SUMMA, JOHN F., New York Medical College, 1958. Doctor Summa was director of cardiology at Waterbury Hospital. Doctor Summa was a member of the New Haven County Medical Association, Connecticut State Medical Society and the American Medical Association. Died July 1, 1991.

WILLIAMS, FRANCIS P.A., New York Medical College, 1944. Doctor Williams was chairman of the Department of Emergency Medicine at Bridgeport Hospital. Doctor Williams was a member of the Fairfield County Medical Association, Connecticut State Medical Society and the American Medical Association. Died July 25, 1991.

WINTERS, JOHN T., University of Pennsylvania, 1931. Doctor Winters was a Surgeon in Hartford from 1947 until his retirement in 1982. Doctor Winters was a member of the Hartford County Medical Association, Connecticut State Medical Society and the American Medical Association. Died July 5, 1991.



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Introduction

DIABETES

SAMUEL S. ENGEL, M.D.

Guest Editor

THE past decade has seen major changes in our approach to the management of diabetes. We have seen diabetes care evolve from a palliative practice focusing on the treatment of microvascular and macrovascular complications to a mode where prevention is the major focus. Three types of prevention strategies exist for diabetes: primary prevention, which includes strategies to delay or prevent the development of the disease; secondary prevention, which focuses on restoring the metabolic milieu to normal in an attempt to prevent the vascular and neuropathic sequelae of diabetes; and tertiary prevention, which emphasizes early detection of complications and identification of high-risk individuals.

In this special issue of *Connecticut Medicine,* we will highlight several of the innovations and concepts which have been central to the recent changes in diabetes management. I would like to thank Lyn Lanoue, Health Program Associate, Center for Chronic Disease, Connecticut Department of Health Services, for her idea to produce this special issue of *Connecticut Medicine* on diabetes, and for her assistance and the assistance of Carol Homko, formerly Diabetes Nurse Clinician at Yale-New Haven Hospital and presently Co-coordinator, Diabetes-in-Pregnancy Program at Temple University. I would like to thank Dr. Robert Massey and Wanda E. Jacques of *Connecticut Medicine* for making this issue possible. Most importantly, I would like to express my gratitude to the authors, most of whom are from Connecticut, for their contributions of time and valuable expertise reflected in the articles in this issue.

Diabetes is a significant public health problem in Connecticut. The Centers for Disease Control (CDC) report Connecticut's average mortality rate for diabetes ranked sixth highest among the 50 states and the District of Columbia for 1980-86.[1] Diabetes was listed as the primary cause of 500 deaths in Connecticut in 1988, and the seventh leading cause of death overall.[2] CDC estimates that, in fact, more than 2,400 Connecticut residents die annually from diabetes and related complications.[3]

Results from the Connecticut Behavioral Risk Factor Surveillance Survey of adults 18 years of age and older for 1988-89 indicate a prevalence of known diabetes of 4.5%.[4] CDC estimates more than 185,000 Connecticut residents have diabetes. Of this number, about 93,000 have been diagnosed.[3] Age-adjusted prevalence rates from all states participating in Behavioral Risk Factor Surveillance System indicate that diabetes is 22% more prevalent in females than in males, and 92% higher in the black and 61% higher in the Hispanic population than in the white population.

Diabetes costs the state of Connecticut approximately $277 million a year in direct and indirect costs. About 39,000 diabetes-related hospitalizations occur annually. It is estimated that more than 1,100 Connecticut citizens suffer significant diabetes-related complications each year including over 795 lower-extremity amputations, more than 120 new cases of end-stage renal disease, and at least 190 new cases of blindness.[3]

Advances in our understanding of the etiology and pathogenesis of the various forms of diabetes have moved medical science closer to the time when high-risk individuals will be identified prior to the development of metabolic disturbances. Dr. Malchoff discusses the current recommendations for diagnosis and classification of diabetes, and the prospects for primary prevention of Type I diabetes in the future. Weight loss strategies in the treatment and prevention of Type II diabetes are reviewed by Ms. Held. The combination of insulin with oral hypoglycemic agents has become increasingly popular in the treatment of Type II diabetes, and Dr. Rosenblatt summarizes the rationale for this approach and the literature supporting the use of combination therapy. Blood glucose testing has replaced urine glucose testing as the preferred method of patient self-monitoring. Dr. Walker discusses issues relating to the quality control of capillary

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blood glucose testing and the utilization of these patient-generated data. Diabetes, perhaps more than any other disease, must involve health professionals from multiple disciplines. The changing roles of the nurse-educator and the dietitian are described in the articles by Homko and by Wylie-Rosett and Engel. In the area of tertiary prevention of chronic complications, practical strategies to limit morbidity from the vascular and neuropathic effects of this disease are reviewed by Dr. Petit. Finally, the current care standards as recommended by the American Diabetes Association are reprinted in this issue.

The past decade has seen dramatic changes in knowledge and attitudes regarding diabetes treatment; we anticipate that this will result, in the years to come, in substantial improvement in the health and well-being of our patients with diabetes.

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Diagnosis and Classification of Diabetes Mellitus

CARL D. MALCHOFF, M.D., PH.D.

DIABETES mellitus is characterized by abnormalities of glucose, fat, and protein metabolism. It is not a disease itself, but rather a final common clinical syndrome caused by diverse etiologies which are incompletely understood. Treatment of diabetes will prevent or delay other acute and chronic complications of altered metabolism. The abnormalities of glucose metabolism and its immediate consequences are the cornerstone of our diagnostic criteria for diabetes mellitus. Classification of diabetes into subgroups is useful for predicting prognosis and therapy; however, our classification criteria are imperfect. Historically, the criteria for diagnosis and classification have emphasized the metabolic abnormalities. This emphasis is shifting to the identification of the causal disorder. I will summarize current criteria for diagnosis and classification, suggest some practical guidelines regarding their clinical use, and indicate possible future directions.

Criteria for the Diagnosis of Diabetes Mellitus

Criteria for the diagnosis of diabetes mellitus, which were established in 1979 by the National Diabetes Data Group (NDDG) of the National Institutes of Health,[1] are outlined in Tables 1 and 2, and have been discussed in detail elsewhere.[2] Similar criteria have been adopted by the World Health Organization[3] and are also acceptable. Although arbitrary, these criteria are sensitive enough to identify those individuals at risk for chronic diabetic complications, but not so inclusive as to classify as diabetic the entire 2.3% of the population with circulating plasma or serum glucose concentrations two standard deviations above the mean. They rely on the measurement of glucose concentrations in plasma or serum obtained from venous blood. For practical purposes, plasma and serum glucose concentrations are interchangeable, and I have chosen to present these as common units with SI units in parentheses.

Since the osmotic effects of severe hyperglycemia can cause polyuria, polydipsia, and blurred vision, these clinical findings should always suggest the diagnosis of diabetes mellitus. In this clinical setting, the diagnosis can be confirmed by a random plasma glucose concentration of 200 mg/dL (11.1 mmol/L) or greater. However, this is the least sensitive method of diagnosing diabetes.

In asymptomatic nonpregnant subjects, diabetes can be established by a fasting (12 h overnight fast) plasma glucose concentration of 140 mg/dL (7.8 mmol/L) or greater on two or more occasions. Normal fasting plasma glucose is less than 115 mg/dL (6.4 mmol/L) following a 10 to 12 h overnight fast. Those individuals with fasting glucose concentrations from 115 mg/dL (6.4 mmol/L) to 139 mg/dL (7.8 mmol/L may be classified as having impaired glucose tolerance (IGT), depending on the results of a glucose tolerance test.

The most sensitive test for diabetes is the oral glucose tolerance test. The methods of performing the test and the normal ranges differ in pregnant women and in other subjects. In nonpregnant subjects the test is performed following a 12 h overnight fast using a 75 g glucose load (1.75 g/kg up to a maximum of 75 g in children) which is dissolved in water and consumed over five min. Venous blood is drawn immediately prior to consumption and at 0.5, 1.0, 1.5, and 2.0 h following initiation of consumption, and the plasma is assayed for glucose. The diagnosis of diabetes is suspected if the two-hour sample and one other postingestion sample are 200 mg/dL (11.1 mmol/L) or greater. The test must be repeated before the diagnosis is established. Impaired glucose tolerance is diagnosed if the glucose level rises above 200 mg/dl during the test, but falls below 200 mg/dl at the two-hour time point.

In all pregnant women a screening oral glucose tolerance test is recommended between weeks 24 and 28 of pregnancy. Plasma glucose is measured immediately before and 1 h after a 50 g glucose load. A fasting con-

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Table 1

Criteria for the Diagnosis of Diabetes Mellitus in Nonpregnant Adults

Test	*Criteria for diabetes (Plasma, glucose, concentrations)*
Random plasma glucose	≥200 mg/dL (11.1 mmol/L) plus symptoms of diabetes
Fasting plasma glucose	≥140 mg/dL (7.8 mmol/L)
Oral glucose tolerance test (75 g glucose load)	≥200 mg/dL (11.1 mmol/L) at 2h and one other time (0.5, 1, or 1.5 h)

centration of 105 mg/dL (5.8 mmol/L) or a 1 h concentration of 140 g/dL (7.8 mmol/L) are indications for a complete oral glucose tolerance test. In pregnant women this is performed with a 100 g glucose load, and blood is drawn at 1, 2, and 3 h. The diagnosis of gestational diabetes is made if two or more of the plasma glucose concentrations meet or exceed the critical concentrations outlined in Table 2.

Correct methodologies and the appropriate clinical setting are necessary to avoid misdiagnosis. Blood should be drawn from a vein for preparation of either serum or plasma. Other sources of blood are not appropriate. Arterial blood and capillary blood have higher glucose concentrations than venous blood, and this difference is exaggerated in the postprandial state. While glucose may be measured in either serum or plasma, it should not be measured in whole blood, since glucose concentrations in whole blood are about 15% lower than concentrations in serum or plasma. Following phlebotomy, care should be taken to prevent the glucose metabolism by the glycolytic enzymes of the cellular elements of blood. Chilling tubes on ice and using flouride tubes both are effective, however, the flouride invalidates the enzymatic measurements of glucose. The glucose tolerance test may yield a false positive result if the subject is at bed rest, has another concomitant illness, or has been eating a low carbohydrate diet. All of these variables cause insulin resistance and may result in an elevated serum glucose following an oral glucose load. Attention to these details will prevent the misdiagnosis of diabetes.

Criteria for the Classification of Diabetes Mellitus

The major classifications of diabetes mellitus are summarized in Table 3. While secondary diabetes represents the minority of the causes of diabetes, it is anticipated that in the future the causes of diabetes will be identifiable in all patients. Currently secondary diabetes is the outcome of a variety of unusual disorders which destroy the pancreatic beta cells, increase counter-regulatory hormones, or produce very severe insulin resistance.

Type I diabetes mellitus, also called insulin-dependent diabetes mellitus (IDDM), was formerly called juvenile-onset diabetes mellitus (JODM) and accounts for about 10% of all diabetic patients. This disorder is generally believed to be due to the autoimmune destruction of pancreatic beta cells, and is associated with anti-islet cell antibodies, anti-insulin antibodies, HLA-DR3 and HLA-DR4 antigens, and with other autoimmune diseases.[4] Generally the onset is before age 35 and insulin therapy is required to prevent ketoacidosis. The predisposition to this disorder is inherited, but the concordance between identical twins is only about 50%, suggesting a possible etiologic role of environment and/or somatic mutation. There is considerable research interest in the early identification of this disorder by analysis of anti-islet cell and anti-insulin antibodies, so that immune modulating therapies can be initiated during the prediabetic state. Measurements of islet cell antibodies are commercially available. However, since their sensitivity is only about 75% in new onset Type I diabetes, they currently have limited clinical utility.

Type II diabetes mellitus, also called noninsulin-dependent diabetes mellitus (NIDDM), was formerly called adult-onset diabetes mellitus (AODM) and accounts for about 90% of all diabetic patients. While obesity, insulin resistance, and impaired insulin secretion are often present, the primary cause remains unknown. Usually the onset is after age 40, and insulin therapy is not required to prevent ketoacidosis. A predisposition to this disorder is inherited, and the concordance between identical twins is nearly 100%. Maturity-onset diabetes of youth (MODY) is a very rare subtype of Type II diabetes which is inherited in an autosomal dominant fashion. Since the onset of diabetes becomes clinically apparent before age 30, MODY can be analyzed by genetic linkage analysis. Current studies suggest that the gene for this disorder is near the adenosine deaminase gene on chromosome 20.[5] It is anticipated that future genetic studies will identify the responsible gene, and subsequently lead to a basic understanding of Type II diabetes in general. Eventually the diagnosis of Type II diabetes may be based on genetic, not metabolic, findings.

Impaired glucose tolerance may be diagnosed in those individuals who do not meet the criteria for diabetes but have an abnormal fasting glucose or glucose tolerance test. About 30% progress to develop diabetes, and about 30% normalize.

Diabetes during pregnancy is classified as gestational diabetes. About 50% of these women may develop Type II diabetes later in life. Not all women developing diabetes during pregnancy have gestational diabetes. Pregnancy offers no protection against the development of Type I diabetes mellitus which occasionally will develop concurrently with the pregnancy.

Among the drugs contributing to the development of the diabetic state, the glucocorticoids are the most common. Pentamidine is a pancreatic toxin and may cause diabetes in up to 20% of individuals receiving it parenterally for the treatment of *Pneumocystis carinii* pneumonia.[6] With the increased prevalence of AIDS the use of pentamidine is increasing, and it is likely that this cause of diabetes will become more common.

Diagnosing Diabetes: Practical Considerations

Testing for diabetes should rely on the methodologies described above. Some have suggested that the hemoglobin A1C or other glycated protein measurements be used to screen for diabetes mellitus. Since these tests are more expensive, less sensitive, and less specific than a fasting serum glucose concentration,[7] my own bias is that they should not be used to screen for or diagnose diabetes. Testing of whole capillary blood using the home glucose-monitoring devices is not appropriate when laboratory analysis of plasma is available. The precision and accuracy of these devices is not equivalent to that of a laboratory with appropriate quality controls, and the tests for diabetes are not standardized for whole capillary blood.

Clinical judgment is required to decide when the tests for diabetes should be applied.[8] The suggestions presented here reflect my own philosophies of patient care. Guidelines for the application of these tests are the same as for the application of any diagnostic test. A test for diabetes mellitus should be performed only if a diagnosis of diabetes mellitus will change the physician's care of that patient. General screening of the pediatric or adult population is probably not indicated.[8] Patients with the classical symptoms of polyuria, polydipsia, and weight loss should be tested for diabetes with a random and/or fasting glucose determinations. If these symptoms are due to diabetes, then these tests will establish a diagnosis which is likely to lead to appropriate therapeutic interventions. The relationship between mild degrees of glucose intolerance and a less than optimal outcome of pregnancy is well established.[9-11] Therefore, it is generally recommended that all pregnant women be screened with the 50 g oral glucose tolerance test during weeks 24 to 28 of pregnancy. If the screening test is positive, then it is necessary to perform the more specific glucose tolerance test using the 100 g oral glucose load with phlebotomies at 0, 1, 2, and 3 h. Appropriate intervention with normalization of glucose concentrations will improve the outcome of the pregnancy. Those patients with disorders potentially caused by or related to the diabetic state should also be tested for diabetes. For instance, individuals with hyperlipidemias should be tested, since treatment of the diabetes is likely to improve the lipid abnormalities. Adults with a strong family history for Type II diabetes who are motivated to invest time and effort in their health maintenance should be tested for diabetes. Finally, it is appropriate to test individuals who wish to know if they have diabetes.

Table 2

Criteria for the Diagnosis of Diabetes in Pregnant Women

Test	*Critical values of plasma glucose*
Screening test (50 g glucose load)	≥ 105 mg/dL (5.8 mmol/L) fasting or ≥ 140 mg/dL (7.8 mmol/L) at 1 h
Oral glucose tolerance test (100 g glucose load)	two or more of the following O h (fast) ≥105 mg/dL (5.8 mmol/L) 1 h ≥190 mg/dL (10.5 mmol/L) 2 h ≥165 mg/dL (9.2 mmol/L) 3 h ≥ 145 mg/dl (8.0 mmol/L)

Judgment should be used when selecting a test for diabetes. The most sensitive test is the glucose tolerance test, while the least sensitive test is the random blood sugar. When diagnosing diabetes, one might expect a positive insensitive test to be more likely to influence therapy than a positive sensitive test. For instance, some argue that a glucose tolerance test is necessary to identify those overweight individuals with diabetes mellitus so that an early weight-loss program can be initiated. Others, myself included, argue that a decision can be made to recommend exercise and weight loss without a glucose tolerance test. Physical examination alone will identify those individuals with excess stores of body fat who would benefit from exercise and diet. Fasting plasma glucose concentrations consistently above 140 mg/dL will identify those at risk for diabetic retinopathy, neuropathy, and nephropathy. I rely on the fasting glucose concentration to diagnose diabetes and rarely use the more cumbersome glucose tolerance test in anyone other than pregnant women.

In summary, the application of testing for diabetes mellitus requires the physician's judgment. If making a diagnosis of diabetes will influence both therapy and outcome, then clearly the tests should be used. Alternatively, if the diagnosis will have no effect on subsequent interventions, then our limited health-care dollars are better spent elsewhere. The indications for testing not only vary with each patient, but also are likely to change in the future as new therapies become available.

Table 3

Classification of Diabetes Mellitus

- Type I Diabetes mellitus
- Type II Diabetes mellitus
- Diabetes caused by other defined conditions (secondary diabetes)
    - Pancreatic disease
    - Counterregulatory hormones
    - Abnormal insulin molecule
    - Insulin receptor abnormalities
    - Anti-insulin receptor antibodies
    - Drug or chemically induced
- Impaired glucose tolerance
- Gestational diabetes

Classifying Diabetes Mellitus: Practical Considerations

Some of the causes of diabetes are well understood. Since the identification of these disorders will significantly alter therapy and improve the ultimate prognosis of the patient, it is my contention that they should be investigated aggressively. A good history and physical examination will provide the clues necessary to direct the search for treatable causes of diabetes mellitus. Pheochromocytoma, Cushing's syndrome, acromegaly, glucagonoma, hemochromatosis, cystic fibrosis, insulin receptor mutations, and anti-insulin receptor antibodies are unusual causes of diabetes. However, they have in common two characteristics: they present with specific clinical characteristics, and they respond to appropriate therapeutic interventions. It is my philosophy that the history and physical examination should reveal or suggest these treatable disorders, and, if indicated, the appropriate biochemical testing should be performed.

The distinction between Type I and Type II diabetes can be useful, but is not always necessary. When the classification of a particular patient is obvious, then it helps to direct therapy. For instance, when the subject is a white, 25-year-old individual with normal body weight, hyperglycemia without ketosis, and a negative family history, then the diagnosis is most likely Type I diabetes; insulin should be recommended. This seemingly slow progression to complete pancreatic beta cell failure is relatively common in individuals with the onset of Type I diabetes after age 20, and early recognition helps to avoid confusion and mistreatment. However, when the classification is not obvious, then therapy is directed by the severity of the metabolic abnormalities. The 65-year-old individual with diabetes who has classical symptoms, who has fallen below ideal body weight, and who has no malignancy or other obvious disorder will require insulin therapy regardless of the classification of diabetes. Insulin is the only therapy with an anabolic effect sufficient to restore muscle and fat stores to normal. In such a case, the metabolic characteristics are much more important in determining treatment than is patient classification. Measurements of islet cell antibodies would be interesting, but would not influence therapy. In my practice I classify patients like this as having "insulin requiring" Type II diabetes. It is actually unclear to me whether they have Type I or Type II diabetes. However, the key phrase is "insulin requiring," which suggests that without insulin, they will become significantly catabolic. Thus, it is not always necessary to distinguish between Type I and Type II diabetes to initiate appropriate treatment.

The current classification of diabetes may not be as useful in the black population and other ethnic or racial groups as it is in the white population.[12,13] Again, attention to metabolic characteristics and the use of a clinical trial may help to direct therapy for each individual patient.

I have made the point that diabetes mellitus is not a disease itself, but rather a common metabolic syndrome caused by diverse etiologies. Unfortunately, we do not understand the underlying disorder in the majority of these patients. The cause(s) of Type II diabetes, the most common type of diabetes, is unknown. Even when it is known, it may be that definitive diagnostic testing will be performed by analysis of the responsible gene(s) rather than measurement of metabolic abnormalities. Autoimmunity plays an important etiologic role in Type I diabetes. While this is likely to influence our therapeutic approach in the future, the diagnosis will probably need to be made in the prediabetic state in order to preserve pancreatic function. Hence it is anticipated that in the future that the emphasis will shift from a metabolic diagnosis of diabetes to a diagnosis of the underlying cause during the prediabetic state.

Summary

The diagnosis of diabetes mellitus is established by history, physical examination, and measurements of serum or plasma glucose concentrations under specific conditions. This disorder represents the final common expression of diverse etiologies which are incompletely understood. The treatable causes of diabetes should be identified, and the appropriate therapy initiated. Distinguishing Type I and Type II diabetes is often useful, but not a necessary prerequisite for initiating therapy. As we begin to understand the underlying causes of diabetes, our emphasis is likely to shift from a diagnosis based on metabolic characteristics to a diagnosis based on etiology.

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Standards of Medical Care for Patients with Diabetes Mellitus

DIABETES CARE

DIABETES is a chronic illness that requires continuing medical care and education to prevent acute complications and to reduce the risk of long-term complications. People with diabetes should receive their treatment and care from physicians with expertise and a special interest in diabetes. The following standards define basic (minimum) medical care for people with diabetes. These standards are not intended to preclude more extensive evaluation and management of the patient. For more detailed information refer to Physician's Guide to Insulin-Dependent (Type I) Diabetes: Diagnosis and Treatment and Physician's Guide to Non-Insulin-Dependent (Type II) Diabetes: Diagnosis and Treatment.

Initial Visit

Medical history. The comprehensive medical history can uncover symptoms that will help establish the diagnosis in the patient with previously unrecognized diabetes. If the diagnosis of diabetes has already been made, the history should confirm the diagnosis, review the previous treatment, help evaluate the present degree of glycemic control, determine the presence or absence of the chronic complications of diabetes, assist in formulating a management plan, and provide a basis for continuing care. Elements of the medical history of particular concern in patients with diabetes include:

- Symptoms and laboratory test results related to the diagnosis of diabetes
- Dietary habits, nutritional status, and weight history; Growth and development in children
- Details of previous treatment programs, including diabetes education
- Current treatment of diabetes, including medications, diet, and results of glucose monitoring
- Exercise history
- Frequency, severity, and cause of acute complications such as ketoacidosis and hypoglycemia
- Prior or current infections, particularly skin, foot, dental, and genitourinary
- Symptoms and treatment of chronic complications associated with diabetes: eye, heart, kidney, nerve, sexual function, peripheral vascular, and cerebral vascular
- Other medications that may affect blood glucose concentration
- Risk factors for atherosclerosis: smoking, hypertension, obesity, hyperlipidemia, and family history
- Psychosocial and economic factors that might influence the management of diabetes
- Family history of diabetes and other endocrine disorders
- Gestational history: hyperglycemia, delivery of an infant weighing >9 lb, toxemia, stillbirth, polyhydramnios, or other complications of pregnancy

Physical examination. A complete physical examination should be performed during the initial evaluation. Individuals with diabetes are at high risk of developing eye, kidney, nerve, cardiac, and vascular complications. Patients with type I (insulin-dependent) diabetes also have an increased frequency of thyroid disease, and all individuals with diabetes are at increased risk of infections. Children may have delayed growth and maturation. Therefore, certain aspects of the physical examination require special attention. These include:

- Height and weight measurement (and comparison to norms in children)
- Sexual maturation staging
- Blood pressure determination (with orthostatic measurements)
- Ophthalmoscopic examination, if possible with dilation
- Thyroid palpation
- Cardiac examination
- Evaluation of pulses (with auscultation)
- Foot examination
- Skin examination (including insulin-injection sites)

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- Neurologic examination
- Dental and periodontal examination

The examiner should also be alert for signs of diseases that can cause secondary diabetes, eg, hemochromatosis, pancreatic disease, and endocrine disorders such as acromegaly and Cushing's syndrome.

Laboratory evaluation. Each patient should undergo laboratory tests that are appropriate to the evaluation of the individual's general medical condition. In addition, certain tests should be obtained to establish the diagnosis of diabetes, determine the degree of glycemic control, and define associated complications and risk factors. These include:

- Fasting plasma glucose: a random plasma glucose may be obtained in an undiagnosed symptomatic patient for diagnostic purposes
- Glycosylated hemoglobin (HbA_1 or HbA_{1C})
- Fasting lipid profile: total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides
- Serum creatinine in adults or if proteinuria is present
- Urinalysis: ketones, glucose, protein, microscopic if indicated; after five years of diabetes or after puberty, total urinary protein excretion should be measured by a microalbuminuria method if available
- Urine culture: if microscopic is abnormal or symptoms are present
- Thyroid function tests (T4 or thyroid-stimulating hormone)
- ECG (in adults)

Management plan. The management plan should be formulated as an individualized therapeutic alliance between the patient/family, the physician, and other members of the health-care team (eg, RN, RD) to achieve the desired level of diabetes control. Consideration must be given to the age of the patient, school or work schedules and conditions, physical activity, eating habits, social situation and personality, and presence of complications of diabetes or other medical conditions. Implementation of the management plan requires that each aspect be understood by the patient and the care provider and that the goals and means be considered realistic. Instructions and plans should be reinforced by providing written material appropriate to the patient/family education level. The management plan should include:

- Statement of goals
- Medications: insulin, oral glucose-lowering agents, antihypertensive, lipid-lowering agents, or other medications as needed
- Individualized nutrition recommendations and instructions, preferably by a dietitian
- Recommendations for life-style changes (eg, exercise, smoking cessation)
- Patient and family education: assessment of knowledge and understanding of diabetes and diabetes management skills; plan for education consistent with the National Standards for Diabetes Patient Education of the American Diabetes Association
- Monitoring instructions: self-monitoring of blood and/ or urine glucose, urine ketones, and use of a record system
- Referral to an eye doctor for a comprehensive eye and visual examination: all patients aged 12-30 years with a diagnosis of diabetes of at least five years duration or over age 30 years at time of diagnosis or any patient with visual symptoms and/or abnormalities
- Consultation for specialized services as indicated
- Agreement on ongoing support and follow-up: return appointment and when and how to contact the physician or other members of the health-care team for problem-solving and crisis management
- For women of childbearing age: discussion of contraception and review of program of diabetes care before and during pregnancy

Continuing Care

A continuing-care plan is an essential feature in the management plan of every patient with diabetes. At each visit, the patient's progress in achieving treatment goals should be evaluated, and problems that have occurred should be reviewed. If goals are not being met, both the goals and the treatment plan need to be reassessed.

Visit Frequency

The frequency of patient visits depends on the type of diabetes, degree of blood glucose control achieved, changes in the treatment regimen, and presence of complications of diabetes or other medical conditions. Patients starting insulin or having a major change in their insulin program may need to be in contact with their care provider as often as daily until glucose control is achieved, the risk of hypoglycemia is low, and the patient is competent to conduct the treatment program. Some patients may require hospitalization for initiation or change of therapy. Contact with the patient after a major modification of the treatment plan should not be delayed more than one week. Patients beginning treatment by diet or oral glucose-lowering agents may need to be contacted weekly until reasonable glucose control is achieved and the patient is competent to conduct the treatment program. Contact with these patients after a major modification of the treatment plan should be no more than one month later.

Regular visits should be scheduled for insulin-treated patients at least quarterly and for other patients at least semiannually. All patients must be taught some method of monitoring glycemic control. In insulin-treated patients, and in non-insulin-treated patients with poor metabolic control, this should be blood glucose testing; in other patients, blood glucose testing may be useful. Patients must be taught to recognize problems with their glucose control and to report problems to the health-care team. They also should be taught to recognize early signs and symptoms of acute and chronic complications and to report these promptly.

Elements of Continuing Care

Medical history. An interim history should assess l) frequency, causes, and severity of hypoglycemia or hyperglycemia; 2) results of regular glucose monitoring; 3) adjustments by the patient of the therapeutic regimen; 4) problems with adherence; 5) symptoms suggesting development of the complications of diabetes; 6) psychosocial status; 7) other medical illnesses; and 8) current medications.

Physical exam. A comprehensive physical examination should be performed annually. A complete eye and visual examination by an eye doctor should be performed at least annually in all patients over 30 years old and in patients between 12 and 30 years of age with a diagnosis of diabetes of at least five years duration.

At every regular visit, the following should be measured: height (until maturity), weight, sexual maturation in adolescents, and blood pressure. Portions of the physical examination that were found to be abnormal on previous visits should be repeated. The feet should be examined routinely. The examination should also be extended to include areas indicated by the interim history.

Laboratory. A glycosylated hemoglobin determination should be performed at least semiannually in all patients and preferably quarterly in insulin-treated patients and in non-insulin-treated patients with poor metabolic control. A fasting plasma glucose test may be useful to judge glycemic control in patients with type II (non-insulin dependent) diabetes. The value obtained from a random plasma glucose test may be useful for comparison with the value obtained simultaneously by the patient using his/her own monitoring systems.

Triglycerides, total cholesterol, and HDL cholesterol should be tested annually in adults and every two years in children.

Routine urinalysis should be performed yearly. After five years duration of diabetes, or after puberty, total urinary protein excretion should be measured yearly, by a microalbuminuria method if possible. If proteinuria is detected, serum creatinine or urea nitrogen concentrations should be measured and glomerular filtration assessed.

Management plan. The plan should be reviewed at each regular visit to determine progress in meeting goals and to identify problems. This review should include nutritional evaluation and weight control, the exercise regimen, the control of blood glucose and desired lipid levels, frequency of hypoglycemia, adherence to all aspects of self-care, assessment of complications, follow-up of referrals, and psychological adjustment. In addition, knowledge of diabetes and self-management skills should be reassessed at least annually.

Intercurrent Illness

The stress of illness frequently aggravates the hyperglycemia of diabetes, and during such illness, blood glucose and urine ketones should be monitored frequently. Marked hyperglycemia requires temporary adjustment of the treatment program, and the patient treated with oral hypoglycemic agents or diet alone may temporarily require insulin. Infection or dehydration is more likely to necessitate hospitalization in the person with diabetes than in the person without diabetes. If possible, the hospitalized patient should be treated by a physician with expertise in the management of diabetes.

Special Considerations

Diabetic ketoacidosis and hyperosmolar coma. These conditions represent decompensation in diabetic control and require immediate treatment. Depending on the severity of the illness and available resources, treatment can be undertaken in the physician's office, emergency room, hospital room, or medical intensive-care unit. Recurrence demands a detailed psychosocial and educational evaluation by a diabetes specialist.

Severe or frequent hypoglycemia. The occurrence of severe, frequent, or unexplained episodes of hypoglycemia requires evaluation of both the management plan and its execution by the patient and may indicate a need to revise the plan or reeducate the patient. The accomplishment of these goals generally requires more frequent patient visits during adjustment of the treatment program.

Pregnancy. To reduce the risk of fetal malformations and maternal and fetal complications, pregnant women and women planning pregnancy require excellent blood glucose control. These women need to be seen by a physician frequently, must be trained in self-monitoring of blood glucose, and may require specialized laboratory and diagnostic tests. Consultation with an obstetrician and medical specialist in diabetes is indicated before pregnancy.

Hypertension. Hypertension contributes to the development and progression of chronic complications of diabetes. Hypertension should be treated aggressively to achieve and maintain blood pressure in the normal range. The selection of an antihypertensive drug should be individualized to minimize the number and severity of side effects. For example, ß-blockers should be used with caution in insulin-treated individuals because these drugs may mask early symptoms of hypoglycemia and prolong recovery from hypoglycemia.

Retinopathy. Diabetic retinopathy or other visual abnormalities require care by an ophthalmologist experienced in the management of people with diabetes.

Nephropathy. The patient with abnormal renal function (proteinuria or elevated serum creatinine) requires heightened attention and control of other risk factors (eg, hypertension, smoking) and requires consultation with a specialist in diabetic renal disease.

Cardiovascular disease. Patients with cardiovascular risk factors should be carefully monitored. Evidence of cardiovascular disease such as angina, decreased pulses, and ECG abnormalities requires efforts aimed at correction of contributing risk factors (eg, obesity, smoking, hypertension, sedentary life-style, hyperlipidemia, poorly regulated diabetes) in addition to specific treatment of the cardiovascular problem.

Neuropathy. Diabetic neuropathy may result in painful paresthesias, muscle weakness, and loss of sensation. Autonomic involvement can affect the function of various organ systems (gastrointestinal, cardiovascular, genitourinary) and may require consultation with an appropriate medical specialist.

Foot care. Problems involving the feet may require care by a podiatrist or other medical professional experienced in the management of people with diabetes. Patients with evidence of sensory neuropathy should be educated about the risk and prevention of foot problems.

Children and adolescents. Children and adolescents with diabetes, especially preschoolers and teenagers, should be managed in consultation with a physician who has expertise in treating children with diabetes.

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Combination Sulfonylurea-Insulin Therapy in the Treatment of Noninsulin-Dependent Diabetes Mellitus

JOSEPH ROSENBLATT, M.D.

COMBINATION therapy of diabetes using insulin with sulfonylureas has become increasingly popular over the past five years. In this article, the rationale for the use of this treatment approach will be discussed, and studies of combination therapy will be reviewed.

There are 15 million people with diabetes in the United States. Approximately 15% have Type I, or insulin dependent diabetes (IDDM), and 80% have Type II, or noninsulin dependent diabetes (NIDDM). The remaining 5% have other secondary forms, such as diabetes due to Cushing's syndrome or hemochromatosis. The hallmark of all forms of diabetes is hyperglycemia and relative or absolute insulin deficiency.

Patients with NIDDM differ from those with IDDM in not only having deficient insulin secretion but also decreased insulin action, or insulin resistance.[1] The insulin resistance results in both decreased uptake of glucose in peripheral tissues as well as decreased suppression of hepatic glucose production. In patients with mild hyperglycemia, the primary abnormality is decreased glucose uptake in muscle cells, resulting in postprandial hyperglycemia. In patients with more severe hyperglycemia, there is also an increase in hepatic gluconeogenesis leading to fasting hyperglycemia.

Insulin resistance is felt to occur at both the insulin receptor and at a postreceptor site. This postreceptor defect is in turn a heterogeneous abnormality, including abnormalities in the generation of the "second messenger" of insulin action, the activation of intracellular enzyme activity, and in glucose transport across cell membranes. Ultimately, all causes of insulin resistance will have a final common clinical expression—an increased requirement for insulin secretion in order to maintain normal serum glucose levels.

Although people with NIDDM are frequently characterized as hyperinsulinemic, when compared with weight-matched controls, they actually have diminished insulin secretory reserve. In patients with mild hyperglycemia, the first phase of the insulin secretion response to carbohydrate is lost. In general, patients with a fasting glucose above 180 mg/dL have abnormalities in both early and late phase insulin secretion. In addition to this decrease in secretion in response to carbohydrate, there may also be a decreased ability of the serum glucose to modulate the insulin secretory response to other stimuli such as dietary protein or other hormones. Several mechanisms for this abnormality have been postulated. A common theory has been beta cell exhaustion: the persistently increased insulin secretory demand results in the beta cells being unable to keep up with the amount of insulin required. A direct toxic effect of glucose on the beta cell has also been suggested.[2] In support of this hypothesis is the observation that improvement of hyperglycemia results in improvement in islet cell function.

Therapy for NIDDM should be directed to the underlying pathophysiology. The fasting blood sugar is determined by the degree of hepatic glucose production. In addition to the insulin resistance that is present in patients with NIDDM, further resistance to insulin action occurs in the several hours preceding and subsequent to waking, often termed the dawn phenomenon. This is primarily related to the nocturnal growth hormone surges which occur during sleep in nondiabetic as well as diabetic adults and children. Thus in NIDDM, there is a combined defect that further increases the fasting blood glucose. The postprandial rise in glucose is related to the varying degrees of resistance to transport of glucose into the peripheral tissues. Thus treatment should be aimed at not only increasing insulin secretion, but also at decreasing insulin resistance.

Accelerated atherosclerosis has long been recognized to be an integral part of the diabetes syndromes in general, and of NIDDM in particular. For example, the Multiple Risk Factor Intervention Trial (MRFIT) demonstrated a

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two- to four-fold increase in coronary artery disease when diabetes was added to other risk factors such as hypertension, elevated cholesterol, and cigarette smoking.[3] In vitro studies have provided a conceptual basis for the observed increase in atherosclerosis in patients with diabetes. Elevated insulin levels have been associated with stimulation of smooth muscle and fibroblast cell growth in vascular tissue. An increase in uptake of lipids in vascular tissue and inhibition of fibrinolysis have also been observed.[4] Hyperinsulinemia has also been found to be associated with hypertension, and may in fact be causal in its development because of effects on sodium metabolism and on vascular sensitivity to endogenous catecholamines. The combination of insulin resistance, hyperinsulinemia, hyperlipidemia, hypertension, and obesity has been referred to as syndrome X, or Reaven's syndrome; hyperinsulinemia is felt to be a major factor in the mechanism of accelerated atherosclerosis and the development of coronary artery disease in this syndrome.[5] Improvement of diabetic control, associated with lowering of insulin levels, may thus be beneficial in limiting the progression of vascular disease and is an important aim of combination therapy of insulin and oral hypoglycemics.

As 80% of patients with NIDDM are obese, weight reduction combined with exercise is the primary therapy. Both weight loss and exercise are associated with decreased insulin resistance and secondary effects on insulin secretion. Thus, the hyperinsulinemia seen in obese Type II diabetic patients can be reversed by these treatment modalities. Unfortunately success at maintaining long-term weight loss has been limited.[6] When diet and exercise are not sufficient to reach treatment goals, pharmacologic therapy is indicated.

The hypoglycemic effect of sulfonylurea drugs had been noted in the 1940s in association with research on sulfonamides for the treatment of typhoid. The first generation oral hypoglycemic agents have been available since the late 1950s and the second generation since the early 1980s. The second generation oral agents, including glyburide and glipizide, along with the first generation agent, chlorpropamide, make up 75% of the United States market. Oral agents are believed to work predominantly by increasing beta cell sensitivity to glucose.[7] They do not directly stimulate insulin secretion. Thus, when a patient is treated with a sulfonylurea, there is an enhanced insulin response to a given blood glucose level. Because of the increased insulin production, the blood sugar is lowered and in turn the amount of insulin secreted is decreased. A new steady state is established with similar, or lower, insulin levels and with lower blood glucose levels. Although it was believed that oral agents also decreased insulin resistance, this is controversial.

An important difference between oral agents and insulin injection therapy is that insulin released in response to oral agents is secreted directly into the portal vein. Insulin administered by subcutaneous injection is absorbed by the peripheral capillary bed and traverses the peripheral venous and arterial circulation before reaching the liver. Thus insulin injection therapy exposes patients to higher peripheral insulin levels in order to maintain therapeutic portal vein insulin levels. Oral agents, by maintaining a portal-peripheral insulin gradient (normally about 4:1), allow for lesser degrees of peripheral hyperinsulinemia and decrease concerns about accelerated atherogenesis.

There is a 20% primary failure rate with oral agents, and approximately a 5% to 10% annual secondary failure rate for patients who were initially controlled on oral agents. Treatment with insulin in divided doses is usually started at this point. In addition to the potential deleterious effects of insulin injection therapy on peripheral hyperinsulinemia, insulin therapy is also associated with an increased potential for hypoglycemia. A recent approach to insulin therapy for patients with NIDDM has involved the use of an intermediate acting insulin at bedtime.[8] This works predominantly in the overnight period to limit hepatic glucose production and improve the fasting blood glucose. With improvement in the fasting glucose level, improved islet cell function in response to meals throughout the day may be anticipated. Nocturnal hypoglycemia is unlikely, especially in view of the dawn phenomenon, which results in an increase in insulin requirement tending to coincide with the peak action of the intermediate duration insulins.

Combination therapy with insulin and oral hypoglycemic agents was suggested as early as 1957 by Fabrykant.[9] The synergistic effect between insulin and the oral agents is such that improved control may be achieved with decreased insulin requirements. This approach would be preferred to high doses of injected insulin because it reduces the potential effect of hyperinsulinemia on accelerated atherosclerosis. Recently there has been a review of approximately 20 studies on combination therapy by Peters.[10] Many of these studies suffer from a short study period (all less than one year), small patient population (usually 10 or less), and nearly all studies using glyburide only. Furthermore, most involved the addition of an oral agent after optimization of insulin therapy had been achieved.

Concurrent trials compared 91 patients with insulin plus placebo versus 93 with insulin plus oral agents. There was minimal improvement with placebo alone. The fasting blood sugar dropped from 204 mg/dL to 169 mg/dL with combination therapy. The glycohemoglobin levels showed a similar improvement and the insulin dosage was decreased with combination therapy from 64 to 48 units.

Crossover trials involved 91 patients and showed similar results with a drop in the mean fasting blood sugar from 198 mg/dL to 162 mg/dL with combination therapy. This was again associated with a drop in glycohemoglobin levels. The insulin dosage decreased from 48 to 41 units per 24 hours. Predictors of a good response to combination therapy included poor initial glycemic control, greater degree of obesity, and shorter duration of diabetes. The predictors were limited in accuracy, however, and a number of patients did worsen on combination therapy. Studies looking at the mechanisms of improved control suggested that the predominant effect was through increased endogenous insulin production, as measured by C-peptide levels. Although peripheral insulin levels were not different in patients being treated with combination therapy from those taking insulin alone, the improvement in the degree of hyperglycemia suggests improvement in insulin resistance. The mechanism of the improved insulin resistance was not determined. In the few studies that examined binding to insulin receptors there was no change.

There are negative aspects of combination therapy. The cost of adding an oral agent is greater than the cost of simply increasing the insulin dose. There is a potential for side effects from the oral agents, although the second generation drugs are usually well tolerated. Finally, combination therapy is more complicated than using insulin alone, and may result in problems with patient compliance.

Normoglycemia has been difficult to obtain for both IDDM and NIDDM. Studies on combination therapy have shown that many patients, but not all, will show a modest degree of improved glycemic control.[9] Whether this improvement in glycemic control, associated with decreased insulin requirements, will result in a decrease in the rate of development of the chronic complications of diabetes remains to be seen.

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The Clinical Utility of Capillary Blood Glucose Monitoring in the 1990s

ELIZABETH ARQUIN WALKER, R.N., D.N.Sc.

ABSTRACT—The purpose of this article is to explore the clinical utility of capillary blood glucose monitoring (BGM) in providing data for management decisions by persons with diabetes and by clinicians in acute and chronic care facilities, as well as in the private practice setting.

Issues that affect clinical utility include: quality assurance for the BGM procedure, knowledge and beliefs regarding BGM of both the patient and the clinician, and communication patterns. Counseling patients regarding the frequency of their self-monitoring should be individualized and based on the type of treatment for managing the patients' blood glucose, their resources, and their motivation for making dietary, medication, or exercise changes based on the BGM results.

Thus, the clinical utility of BGM is dependent on the quality of data generated and the utilization of these data for management decisions by informed and motivated patients and clinicians.

Introduction

CAPILLARY blood glucose monitoring (BGM) is the measurement of one parameter of a patient's current metabolic status for diabetes management. The technology of BGM has become a pivotal component of the therapeutic regimen for diabetes because it can provide rapid blood glucose test results of sufficient reliability for clinical decision-making by either patient or clinician.[1-3] Self-monitoring may be a powerful tool to reinforce positive health behaviors; patients are able to obtain immediate feedback related to changes in dietary, exercise, or medication changes.[4] While this technology provides the clinician with another monitoring tool for diabetes, it must not be utilized as a diagnostic tool.

Self-monitoring of blood glucose is considered a standard of care for insulin-dependent and insulin-requiring patients with diabetes. It should also be considered a treatment option for anyone with diabetes who is able to perform the test and is motivated to use the test results.[5]

Research related to BGM in the 1980s focused on accuracy and reliability of BGM systems,[6,7] benefits of self-monitoring for patients,[8,9] and to a lesser extent, the clinical significance of error in BGM.[3,10] The early expectation that BGM by patients would lead unilaterally to improved metabolic control has been replaced by a more realistic emphasis on self-monitoring as an essential component of a complex therapeutic regimen.[11]

In the 1990s, the clinical utility of BGM will be seen as an outgrowth of knowledgeable utilization of accurate data by both patient and clinician. Factors that either promote or impede the clinical utility of BGM include approaches to quality assurance and patient-clinician data utilization.

Quality Assurance in BGM

Quality assurance can be defined as "a comprehensive program designed to ensure proper performance of each step of the procedure leading to a reliable result."[12] Capturing accurate, reliable BGM data is dependent on the total system—the user (patient or clinician), the instrument (monitor/meter), and other components used to perform the test (fingerstick device, reagent strips, etc.). The concept of quality assurance for BGM performed by both patients and clinicians is widely accepted; the practice of measures for quality assurance is less a reality.

Patient Use—The proliferation in the 1980s of BGM devices for patient use has created a market in which patients can purchase monitors without individualized instruction in their use from pharmacies, through mail order, and from other retail establishments. While ease of purchase of monitors has its advantages for patients, information concerning quality assurance for the test may not be available to patients. Unfortunately, most clinicians would not be surprised to discover that patients have

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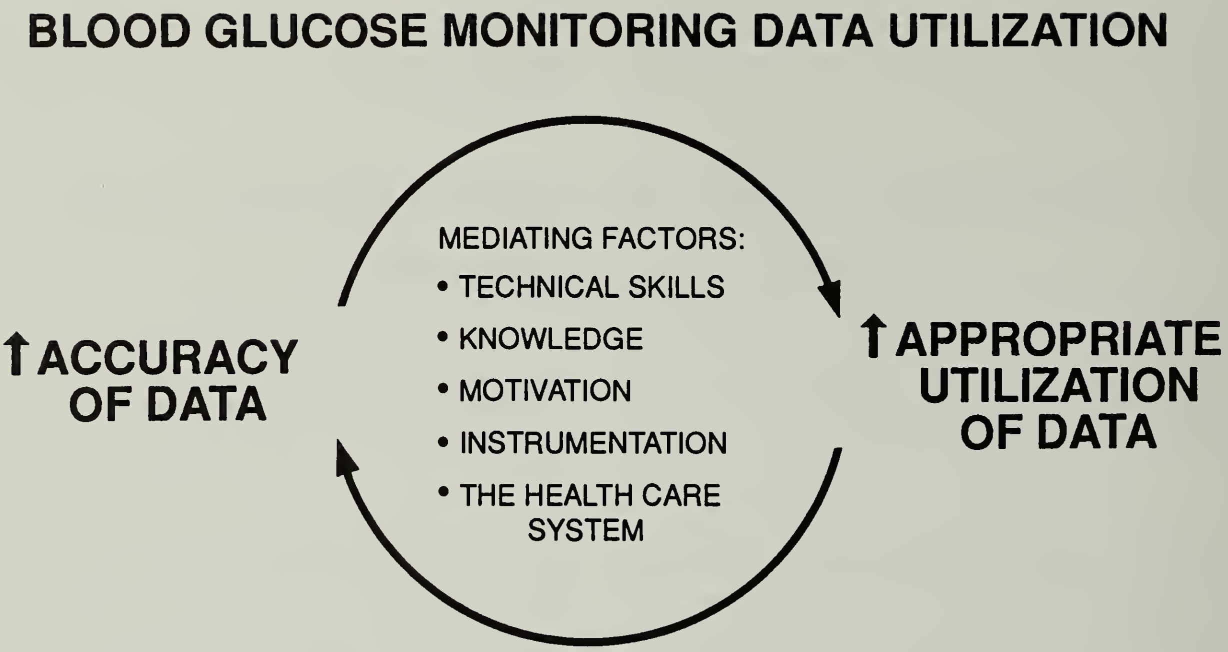

Figure 1

never heard of aqueous glucose solutions for quality control tests; have never cleaned their monitors; or did not realize that reagent strips have an expiration date. Thus, access to comprehensive initial training in the BGM technique and to periodic reassessment of patient skills by a clinician or trainer must be an integral part of the quality assurance program for patients. See Table 1 for common sources of error in the BGM technique. There are limited data concerning the degree to which each source of error may contribute to inaccuracy that is of clinical significance to patients' health outcomes.[13]

Because BGM systems continue to be technique-dependent, the clinical utility is directly related to the quality assurance built into the patient's use of this technology. In other words, patients must learn how to use the system properly and how to problem-solve system errors. Periodic review of patients' technique and quality assurance practices is essential. Although most BGM systems come with self-instructional materials, patients must demonstrate proper technique to their health care providers. The QA challenges for clinicians are to provide time and trained staff to teach and/or evaluate patient technique during an office visit, and to encourage patients to bring monitoring equipment and BGM records at scheduled visits.

Clinician Use—There are multiple standards for quality assurance for capillary BGM performed by clinicians in health care facilities. Both state and national regulatory and accrediting agencies have standards that are not always consistent with each other.[12,14-16] Many acute and chronic care settings provide bedside BGM services for assessing patients, and these services are generally coordinated by nursing and/or the clinical laboratory.[17] Because the quality assurance guidelines developed less rapidly than the technology, many facilities in the 1980s provided the BGM service with no formal quality assurance program.

The regulations for the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88, Public Law 578) may have profound ramifications for BGM in health care facilities and other test sites, such as physician offices, schools, diabetes camps, and home health care settings.[18] The final Health Care Financing Administration (HCFA) regulations are pending, with the uncertainty centering on the classification of BGM performed with a monitor (visually-read reagent strips are considered waivered) as a Level I laboratory test. As a Level I test, BGM with a monitor would be subject to specific personnel requirements, routine inspections, a periodic fee to cover government expenses, as well as quality control and proficiency testing requirements.[18] Professional organizations concerned with diabetes have requested HCFA to classify all capillary blood glucose monitoring as a waivered laboratory test. It is important to note that patient use of monitors is not covered by the CLIA '88 regulations.

The clinical utility of capillary BGM by clinicians in various health care settings is obviously dependent on the assurance of "good data" for therapeutic decisions. The same concerns about training of users, periodic review of technique, and other quality assurance measures apply to all health care providers, as they did to patient users. Significant differences are that blood glucose monitors in health care facilities may have multiple users and the health of the person being tested is generally in a compromised state. Quality assurance programs that meet regulatory and accrediting agency requirements can be cost prohibitive for health care facilities, unless the costs can be retrieved by charging patients for the service.

The expertise required to manage a quality assurance program for BGM in health care facilities is drawn from nursing, medicine, and the laboratory, with the cooperation of hospital administration, infection control, and central supply or the pharmacy.[17] The benefits of providing bedside BGM must be weighed against the costs of staff time, quality assurance, materials, and documentation of the process. A program that meets both patient needs and regulatory requirements is labor-intensive. For optimum clinical utility, BGM must be a multidisciplinary endeavor in health care facilities. A secondary gain for the collaborative programs is that clinicians and laboratorians learn each other's "language" and priorities.

Patient-Clinician Data Utilization

Data Utilization Model—A second factor that can either promote or impede the clinical utility of BGM is the utilization of the data by both clinicians and patients. Appropriate data utilization is mediated through a multifactorial process (Figure 1) and is directly related to the accuracy of the data. This model is based on two questions often posed by clinicians concerning BGM: Why bother with all the quality assurance if the data are not used? and Why use data that you don't think are accurate?

The data utilization model postulates that the greater the accuracy (or perceived accuracy) of the BGM data, the greater the appropriate utilization of these data that is trusted. Increased accuracy, however, is dependent upon knowledge and skill in test technique and quality assurance protocols, design of the monitor (ease of use), motivation of the user to perform the test as specified by the manufacturer, and support of the user by the health care system. On the other hand, increased appropriate data utilization depends on knowledge of proper clinical decisions based on the data, motivation to look for patterns and to request additional information, use of computerized data management systems with monitors that have a memory, and again, the support of the health care system to gain the time to evaluate patients' data.[19]

Data Utilization By Patients.—In order to use BGM information effectively for self-management, patients and clinicians must agree on the following: (a) frequency of testing, (b) specific times of the day to perform the test, (c) method of recording the results, (d) individualized blood glucose goals for each test, and (e) instructions for adjusting diet, medication, or activity based on the results.[1]

Clinicians consider the type of diabetes, the level of metabolic control desired, and the treatment plan, along with many other variables, when making recommendations to the patient. The BGM goals of a 60-year-old obese male with Type II diabetes will be different from those of a 24-year-old pregnant woman with Type I diabetes. The level of motivation for self-monitoring may also be variable; individuals need to know the reason for their specific self-monitoring recommendations. Fabrication of BG values by patients is a problem which was identified in the mid-1980s;[20] a clear understanding of the purpose of BGM and utilization of the data, as well as the proliferation of monitors with extensive memory, may decrease this tendency. Patients who use monitors with memories should be encouraged to retrieve the data and record it, possibly each week, so that they can assess patterns in their blood glucose results for the recent past.

Self-monitoring data utilization by patients generally improves with time and experience; the direct benefits of BGM during periods of illness or in the investigation of symptoms of hypoglycemia may be seen by patients as ways to avoid hospitalization or a phone call to 911. Appropriate utilization of data with positive outcomes for the patient can reinforce BGM practices. The clinician's challenge is to support patients who attempt to follow a complex regimen and yet their BGM results do not reflect this effort.

Thus, the clinical utility of BGM for patients is dependent of the patient's knowledge and skills in interpreting and acting on the results appropriately. In the 1990s, technologic advances will include the refinement of noninvasive methods (eg, use of near infrared beams) for assessing blood glucose,[21] and further development of data management systems to assist patients in self-management decisions. The patient's ability to assess metabolic status throughout the day, to keep records, and to be able to reproduce these data for instance-by-instance

Table 1

Common Sources of Inaccuracy in BGM

- Improper timing of the procedure
- Inadequate blood sample size
- Inappropriate blotting or wiping of blood from strip
- Monitor or strips exposed to extreme temperatures
- Dirt on optic window of monitor

Table 2

Assessing Blood Glucose Monitoring Data

- Choose a monitering record/log book which is easy for both of you to read.
- Ask a patient to point out significant BGM events or problem times of the day; agree on a way to "tag" these events.
- Look for patterns in relatively normal, recent weeks.
- Use some system to peruse values; eg, fasting → premeal → postmeal → bedtime; potential causes of problems, possible solutions.

review, may make the difference in the 1990s for those persons who presently face job discrimination (eg, the armed forces, air traffic controllers, interstate truck drivers) because of insulin-dependent diabetes (R. Ratner, personal communication, 12 September 1991).

Data Utilization by Clinicians—There is a reciprocal relationship between patient and clinician related to BGM; most patients generate the data with the assumption that someone will peruse and interpret patterns and discuss changes in the regimen. Therefore, a corollary of the standard of care that persons who take insulin should self-monitor their blood glucose is that clinicians who care for these patients should respond to the presentation of this data.

Assessing monitoring records can be time-consuming for the clinician unless some method for data management has been utilized. Monitors with memory chips can be down-loaded and the data manipulated through various software programs available from monitor manufacturers. Table 2 is a summary of practical suggestions for assessing BGM records when there is no data management system and the patient is waiting for a response. BGM goals for the time(s) of the day the patient has agreed to test must be specified; variation in the treatment goals is individualized from general guidelines.[22-24] Medical practices with large caseloads of patients with diabetes would benefit from collaboration with a certified diabetes educator (C.D.E.) for those patients who are self-monitoring.

Summary

The usefulness of patient and clinician monitoring of blood glucose relies on the production of accurate test results and appropriate use of these results to make therapeutic decisions. When a patient is asked to perform BGM, a reciprocal relationship is formed in which both patient and clinician have responsibilities and expectations. Skill, knowledge, and motivation are needed to continue the therapeutic process; clear communication of shared goals is key.

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Nutritional Management for Patients with Diabetes

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CONSUMER demand for nutritional advice can be overwhelming for physicians who have had limited nutrition education in medical school. The gap thus created leaves the physician largely unequipped to counter the wealth of misinformation to which patients are exposed. More recently, physicians face increasingly sophisticated questions about the proliferation of new products developed to appeal to the nutritionally concerned consumer. Though diet is universally recognized as crucial to diabetes therapy, many physicians feel uncomfortable explaining exchange lists or answering the wide range of questions that patients ask. Too often, dietary advice is limited to a few sessions at time of diagnosis for the Type I (insulin-dependent) patient and general advice for persons with Type II (noninsulin dependent) diabetes to lose weight and avoid fat and sugar. There are a wide range of approaches to dietary management that may be used with patients who have diabetes. The diabetic exchange list system may not be suited to all patients or appropriate in all practice settings.

Compared to diabetologists in a team practice who make extensive use of the nutritionist's special abilities, resources, and knowledge, the primary care physician may find it more difficult to refer to a dietitian. One barrier may be lack of access to a nutritionist with whom the physician feels comfortable. Poor past experience, lack of knowledge about the services a dietitian should provide, or misinformation about criteria for referral may also contribute.

It is the purpose of this report on nutrition to encourage greater physician use of dietary services. The first section will focus on how to coordinate medical and nutritional care. What role can the physician in a busy practice realistically serve? Which patients need referral? What is the most sensible division of responsibilities between medical and nutritional professionals? Finally, how can a physician find a dietitian whose qualifications and practice philosophy are consistent with his or her own?

The second part of the article will illustrate the scope of services a dietitian should provide. A sampling of nutritional strategies is shown, and currently accepted dietary standards are outlined.

Coordinating Medical and Nutritional Care

Criteria for Referral: Who Needs a Dietitian? Most patients can benefit from dietary help, but in some situations. such as renal failure, hyperlipidemia, or hypertension, nutritional guidance is critical. It is equally important in gestational diabetes, when a diabetic pregnancy occurs in adolescence, or when pregnancy is complicated by obesity or chronic malnourishment. In fact, if a pregnant diabetic patient is not normoglycemic, she should be promptly referred to a dietitian, since normal blood glucose levels are critical to a successful outcome. Diet counseling is strongly advised in certain normal states characterized by altered nutritional needs: lactation, childhood, and adolescence, for example.

Adherence to therapy has been shown to be better when patients are referred to a dietitian at diagnosis. The meal plan can be individualized, the patient helped with weight loss, if necessary, and understanding of the regimen can be ensured. Yearly reevaluation is advisable, especially when there is any major change in lifestyle (job, travel, insulin injections, etc.)

Does a well-controlled patient with diabetes who is otherwise in good health need nutritional evaluation? There are two important reasons for assessment when diet has not been recently evaluated. First, if the patient is eating a high-fat diet, there may be good glycemic control at the price of significant cardiovascular risk. Current standards of care suggest liberalizing carbohydrates from under 40% to up to 60% of calories and reducing dietary fats to approximately 30%. Second, the patient's life may be hampered by adherence to an unnecessarily rigid diabetes program. Today, self-monitoring of blood glu-

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Table 1

Estimation of Desirable Body Weight

Adult Women
100 pounds for the first five feet of height
five pounds per inch for each inch above five feet

Adult Men
106 pounds for the first five feet of height
six pounds per inch for each inch above five feet

Subtract 10% for small body frame
Add 10% for large body frame

Children
Consult growth curves

cose and multiple insulin injections allow greater flexibility of scheduling for patients who desire it, along with improved glycemic control.

Finally, nutritional consultation may help to pinpoint the source of glycemic instability or to unravel other problems in diabetes management. For example, unexpectedly high postprandial blood glucose may arise from consumption of some complex carbohydrate with a high glycemic index (such as potatoes or white bread) that the physician would be unlikely to suspect.

Phase I: The Physician's Role in Nutritional Management.—Generally speaking, nutritional management may be divided into two phases; the first phase, screening and goal setting, is the physician's responsibility, and the second, implementation, falls to the dietitian.

The initial phase involves the recognition of problem areas and patient selection, and should be carried out by the physician according to the criteria above. Weight should be evaluated in relation to height and body frame (see Table 1), and the goals of treatment (eg, weight loss and lower blood pressure), clearly specified. Formulation of a "diet prescription" consisting of calorie allowance and its distribution into protein, fat, and carbohydrate is the physician's next step (outlined below).

Caloric needs will vary depending on growth, pregnancy, activity, and desired change in body weight. Patients close to desirable body weight will need a maintenance calorie allowance, which can be estimated by using Table 2. For patients 20% or more above desirable body weight, a hypocaloric diet will need to be prescribed; a reduction of 500-1,000 calories per day is usual and should result in weight loss of one to two pounds per week. For those who are significantly underweight, supplemental calories should be ordered. Approximately 500 calories a day are needed to gain one pound in a week.

The calorie goal for weight loss should achieve a loss of 1-2 pounds per week. For most adults, a minimal calorie intake of 1,200 calories is needed to meet requirements of essential nutrients.

Table 3 illustrates the distribution of macronutrients in grams based on 50% carbohydrate, 30% fat, and 20% protein, for a variety of caloric levels. These are the proportions currently recommended by the American Diabetes Association and other organizations. In special situations, a departure from this distribution may be necessary. In hypercholesterolemia, fats are usually lowered to between 20% and 30%, with an emphasis on polyunsaturated fats and a reduction in dietary cholesterol. Patients with renal insufficiency may be restricted to a protein intake as low as 0.5 g/kg body weight, or 0.25 g/lb body weight. For hypertension, weight loss and restriction of sodium to 2,000 mg may be needed.

It is preferable if the physician supervises the basic education of the diabetic patient. For the insulin-treated patient, minimal knowledge should include understanding of the need to synchronize insulin action with food consumption, as well as an appreciation of the effect of concentrated carbohydrates on blood glucose. Indeed, during this educational process, a mismatch of timing of insulin administration with the patient's eating pattern often becomes apparent. For the obese patient with Type II diabetes, the relation between excess body weight and glucose intolerance should be explained and the efficacy of even modest degrees of weight reduction in improving diabetes control needs to be emphasized. Many patients still believe that a diabetic diet must be low in carbohydrate, and thus eat many high-fat foods.

The second phase of nutritional management focuses on the dietitian. It consists of an in-depth assessment of eating patterns and the implementation of specific modifications, as well as ongoing education and reassess-

Table 2

Estimated Calories for Maintaining Current Weight if at Desirable Weight

	*Kcal required/ lb. DBW**
Most men and very physically active women under 55 years of age	14-15
Moderately active women, sedentary men under 55 years of age	12-13
Obese individuals, sedentary adults ≥ 55 years of age and younger sedentary adults	10-11

* For overweight individuals, the caloric deficit for achieving weight loss can be estimated by subtracting the caloric requirement based on actual weight from the required maintained desirable body weight.

Table 3

Distribution of Macronutrients

Based on 50% CHO, 30% Fat, 20% Pro

Calories	*CHO (grams)*	*Fat (grams)*	*Pro (grams)*
1000	125	33	50
1200	150	40	60
1400	175	47	70
1600	200	54	80
1800	225	60	90
2000	250	67	100
2500	312	83	125

ment. In some practices, a diabetes nurse specialist may take on a role that is intermediate between physician and dietitian, although patients who have many dietary restrictions or many questions about food composition should be referred to a dietitian.

Phase II: The Role of the Dietitian.—Before implementing the diet prescription, the dietitian should assess the overall goals for nutritional management, paying special attention to adequacy of caloric intake and macronutrient distribution. The physician should be consulted if the plan needs modification or appears unachieveable.

Diet counseling can usually be accomplished in three sessions. The first is devoted to history taking and goal setting, the next two to teaching. Patients who need to lose weight may take more time, as they need support and reinforcement over a longer period.

The nutritionist will evaluate the patient for "predictors of compliance." These include external obstacles to and supports for dietary change, as well as patient strengths and weaknesses that may affect ability to achieve the desired goals. A complete history will also include questioning about the involvement of others in food selection, preparation, and consumption—information that should provide insight into the patient's ability to adhere to a diet. Structural obstacles such as work schedules will also be considered. After evaluation, the dietitian will have a good idea of the likelihood of success.

Another aspect of patient assessment involves deciding on the most appropriate educational approach. Many patients are taught to use the American Diabetes Association exchange lists, while others find more success using a system of counting calories or matching carbohydrate intake with insulin dose.

After assessment is completed, teaching can begin. Food composition, effect of specific foods on diabetes control, and methods of behavior modification form the basis of counseling sessions. Patients, progress is monitored using a variety of tools, including the diet record, the 24-hour recall, a diary of specific behaviors, and achievement of treatment objectives such as a target weight, blood pressure, blood glucose level, or glycosylated hemoglobin concentration.

Effective communication between medical staff and the dietitian is critical. The dietitian must be provided with information regarding medical problems such as hypertension or hyperlipidemia. When evaluation is complete, the dietitian should contact the referring physician promptly. The report may be given by telephone, but we have found that it is more desirable to use a written consultation report, which has the added advantage of becoming a part of the patient's permanent medical record.

Finding the Right Dietitian.—A problem that physicians face is determining whether a person practicing "nutrition" has the appropriate qualifications and expertise.

Varying degrees of competence can be found among individuals who offer nutritional counseling. A registered dietitian (R.D.) with a special interest in diabetes is the best choice. The registered dietitian will have at least a bachelor's degree, and sometimes a master's degree, with course work in biochemistry, physiology, food science, and counseling techniques. Credentials must be reviewed by the Commission of Dietetic Registration of the American Dietetic Association, and the candidate must pass a qualifying written examination. Finally, a minimum of six months of clinical experience supervised by a registered dietitian is required.

The dietitian should be familiar with the use of multiple insulin injection regimens and capillary blood glucose monitoring. Acquaintance with the chronic complications of diabetes and the dietary strategies to prevent and treat them is a must. Many dietitians attend continuing education courses to develop and maintain expertise in diabetes management.

After finding a qualified dietitian, the physician will want to be sure their approaches are compatible. A physician who is most comfortable with exchange lists, for example, may not want to refer patients to a dietitian who uses calorie counting as a counseling method.

Many hospital-based dietitians are available for outpatient dietary consultation, and may be contacted through a hospital dietary department or nutrition support service. Fees vary widely, though sometimes consultations are provided free of charge. In the hospital, a written referral is usually necessary, and the services may be limited to patients referred by physicians on staff. Third-party reimbursement is not generally available for nutrition counseling. However, with a physician letter indicating that it

Table 4

Modifying Diet to Cut Calories

Usual Day's Menu	*Calories*	*Substitute*	*Calories*	*Calories Saved*
Breakfast:				
Orange juice, 1/2 cup	56	1/2 cup orange juice	56	0
2 glazed donuts, jelly filled	552	2 small bran muffins	224	328
1 cup coffee	—	1 cup coffee	—	—
powdered creamer, 2 tbsp	64	skim milk powder, 2 tbsp	28	36
sugar, 2 tsp	30	artificial sweetener	0	30
Lunch:				
4 oz salami sandwich w/mustard	615	4 oz boiled ham w/mustard	345	270
Cola, 12 oz	156	Diet cola	0	156
Snack:				
Handful of chips (1 cup)	91	Small pretzel thins (10)	20	71
1 cocktail (Martini, 4 oz)	160	Wine, 4 oz	101	59
Dinner:				
Strip steakette, 6 oz (cooked)	444	Flank steak, 6 oz	334	110
Baked potato	145	Baked potato	145	0
sour cream, 3 tbsp	93	sour cream, 2 tbsp	62	31
Tossed salad	30	Tossed salad	30	0
blue cheese dressing, 2 tbsp	148	Italian dressing, 1 tbsp	68	80
Green beans, 1 cup in butter sauce	104	Green beans, 1 cup plain	34	70
9:00 P.M.				
Ice cream, 1/2 cup	175	Diet gelatin	0	175
11:00 P.M.				
Candy corn, 1/4 cup	182	Reg. popcorn, 2 cups	128	54
Total Calories:	3045		1575	1470

is a "medical necessity," some insurance companies have covered dietary services.

An increasing number of dietitians have private practices in addition to their hospital work, with counseling done in the evenings or on weekends. Fees are usually slightly higher than hospital-based consultations in the same area, though the fee often includes a two-visit initial consultation.

The American Dietetic Association maintains a list of dietitians who are in private practice. Local affiliates of the American Diabetes Association may also have suggestions. For these, check your local phone directory or dial 1-800-ADA-DISC (232-3472), the national headquarters. County or state dietetic associations and health departments often keep a record of persons who provide dietary counseling.

Common Problems in Nutrition

The second part of this article will include a brief review of some key concepts in nutritional management of diabetes—weight loss as the first order of business in NIDDM, or sodium restriction and weight loss in hypertension; the second goal is to illustrate by case studies and sample menus the wide range of dietary services available.

Managing Diabetes Today.—Fundamentals in the management of both Type I and Type II diabetes include the following: limitation of concentrated sweets; keeping dietary fat to no more than 30% of calories; increased use of "complex" carbohydrates and fiber-containing foods, when possible.

Changes in diabetes therapy during the past decade have been few but important. Knowledge about the glycemic effect of carbohydrates has increased; contrary to accepted thinking, there appears to be no sharp division into "simple" and "complex" carbohydrates. Experimental data show a more complicated picture, with much overlap between the two groups. A "glycemic index," or ranking of foods according to their ability to raise blood sugar, has been developed and, though preliminary, may be used by the dietitian to trouble-shoot and to fine-tune food choices. Another recent finding is that fiber, too, exerts a moderating influence on postprandial blood glucose excursions. Diets high in soluble fibers like guar and pectin, and possible fiber supplements, constitute another potential dietary tool. Finally, current dietary management should incorporate newer technologies in diabetes therapy, when these are appropriate, to improve diabetes control and lifestyle.

Type II Diabetes.—Noninsulin-dependent diabetes probably results from combined insulin resistance and relative insulin deficiency. Between 60% and 90% of individuals with Type II diabetes are obese; for these patients, the primary goal is weight loss. Though long-term success is difficult to achieve, it is most likely when weight loss is gradual, especially if linked to a program of behavior modification.

Case 1. A 43-year-old advertising executive was discovered to have fasting hyperglycemia in the course of her routine physical examination. At 64 inches and 165 pounds, she was 38% above her desirable body weight. Her physician gave her an 1,800-calorie exchange list diet plan, but she found it difficult to follow and she gained two pounds.

She was referred to a dietician, who assessed her personality, eating patterns, and preferences. Based on this information, three strategies were identified as likely to help her lose weight: 1. Substitute meats lower in fat for those with a high fat content (eg, flank steak for strip steak); 2. Limit portion size (eg, of dressings and sauces); 3. Reduce sucrose through the use of sugar substitutes (eg, diet sodas). Modifying her dietary pattern as shown in Table 4 allowed the patient to reduce her daily calorie intake. Note that timing and general components of meals and snacks were similar to those the patient was accustomed to.

Type I Diabetes.—For those with insulin-dependent diabetes, meal composition, timing, and calorie distribution should be kept approximately the same from day to day. Insulin action should be synchronized with exercise and food intake.

Case 2. A 24-year-old woman with Type I diabetes had been managed for several years on a dose of 56 units of NPH insulin at 8 AM and an injection of 22 units at 6 PM. She noted a 26-pound weight gain in the three-year period since initiation of the second daily injection. Her height is 64 inches and her current weight is 146 pounds. She reported frequent night-time eating binges, typically at 2 AM, which she associates with stress induced by her job. She stated that she ate three meals and two snacks daily, that she tried to be consistent in regard to both timing and composition, and that she tested blood glucose twice a day. If meals or snacks were delayed by more than 30 minutes, she experienced severe hypoglycemic reactions, the frequency of which recently increased.

She was referred for dietary counseling and was advised to test blood glucose more often to obtain a fuller glycemic picture. Self-monitoring revealed low blood glucose levels at 2 AM as well as occasional preprandial hypoglycemia. It became apparent that the peaks of insulin action were not synchronous with food intake, and when questioned she reported that since a job change three years earlier, her schedule had been erratic.

A smaller dose of intermediate-acting insulin in conjunction with preprandial doses of short-acting insulin might better suit this woman's somewhat unpredictable lifestyle. The middle-of-the-night insulin reactions probably resulted from too much evening NPH or too early an injection time. These led to night-time eating binges and consequent weight gain.

The patient's physician altered the insulin dose to a split-mix regimen consisting of 28 units of NPH and 10 units of regular before breakfast and 12 units NPH and 12 units regular before dinner. On this regimen, her weight decreased and she had no more hypoglycemic reactions.

Special Problems in Management of Diabetes

Hyperlipidemia.—Hyperlipidemia is common in poorly controlled diabetes and is a function, in part, of metabolic derangement. Primary therapy involves optimizing diabetes control, reducing fat calories to 20%-30%, and substituting polyunsaturated for saturated fats where possible.

Case 3. A 42-year-old man who had had diabetes since he was 16 was admitted to the hospital with a myocardial infarction. Until his hospitalization, he had been in good health except for diabetes, though he seldom visited his physician. His diabetes had been managed by two injections of NPH insulin daily; a glycosylated hemoglobin of 8%, measured a few months before his heart attack, indicated adequate glycemic control. The patient reported no history of insulin reactions nor episodes of ketoacidosis.

The hospital dietitian found that the patient had faithfully followed a meal plan given to him many years before at the time of diagnosis, a plan consisting of nearly 40% of calories derived from fat; the customary fat sources were red meat and cheese.

The dietitian adjusted his diet to include only 30% of fat calories and a higher allowance of carbohydrate. The patient was taught about different fat sources and low-fat methods of meal preparation, such as the use of a nonstick pan.

Hypertension.—Aggressive treatment of hypertension is important in the diabetic patient because of its effects on retinopathy, nephropathy, and macrovascular disease. The first steps in care are to lower sodium to 2g per day and try to reduce weight. Drug therapy should be introduced if conservative methods do not completely normalize blood pressure. (See Case 4 below.)

Renal Failure.—Recent evidence has suggested that a low-protein diet may retard the rate of renal failure. Accordingly, some physicians recommend diets restricted in protein for patients with early diabetic nephropathy.

Case 4. A 28-year-old graduate student with Type I diabetes was found to be proteinuric on routine urinalysis. He was 71 inches tall and weighed 176 pounds; his blood pressure was 145/90. A glycosylated hemoglobin of 10% showed fair diabetes control on his regimen of 18 units NPH and 6 units regular insulin before breakfast and 10 units NPH and 6 units regular before dinner. His urine tests were always negative for glucose and ketones. A 24-hour urine collection contained 2.3 of protein.

Some months before, the patient had begun to test his blood glucose and noted that many values were in the 180-225 mg/dl range. In an attempt to improve his glucose control, he had changed to a low-carbohydrate, high-protein diet. When he was referred to a dietitian for evaluation of sodium and protein intake, it was found that his diet included large quantities of cured meats and cheese. Sodium intake was estimated to be in excess of 7g per day, three or four times higher than the amount usually recommended in management of hypertension. His daily consumption of protein amounted to 160g, or about 2g per kilogram of body weight, three to four times the quantity that should be used in renal insufficiency.

For this patient, a low sodium diet would help his diastolic blood pressure. By eliminating processed foods such as cured meats, cheese, snack foods, canned soups, and fast food meals, he could reduce his sodium intake to the range of 2 g per day. He is unlikely to make such a drastic dietary change, however, without help; a dietitian could suggest food preparation ideas and alternative selections to make eating interesting.

A 40-60 protein diet would provide 0.5-0.75 g/kg—an amount under the 0.8 g/kg recommended daily allowance but above the range in which muscle wasting, cardiac muscle atrophy, and other evidence of protein malnutrition is common. It is inadvisable to reduce protein below 0.5 g/kg. Foods for this patient will have to be carefully chosen in regard to both nutritive value and individual preference, and alterations may be necessary during stress or surgery. Ordinarily a low-protein diet is high in complex carbohydrates selected for palatability and micronutrient content. When albumin excretion falls below 3.5 g/L, one must balance the need to preserve kidney function against the dangers of protein malnutrition.

Conclusion

A diet that fits individual preferences is likely to be followed. For some patients, this may mean including a favorite food, like bacon, or chocolate cake into the meal plan. For others, it may entail getting the answer to some esoteric bit of dietary information: Is swordfish kosher? Are there exchange lists of East Indian foods, diet instructions in Chinese? For those trying to lose weight, emotional support may be as crucial as dietary instruction. The dietitian's role in diabetes, though often viewed as limited to managing the complexities of renal failure or the challenge of the massively obese, is in fact as varied as the patients themselves.

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Weight Loss Strategies in Diabetes

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OBESITY is a strong risk factor for developing non-insulin dependent diabetes (NIDDM). There is a direct relationship between the incidence of NIDDM and the degree and duration of obesity. In the population 40% above desirable body weight (DBW) NIDDM is three times more prevalent than in the population at or below DBW. Futhermore, 80-90% of individuals with NIDDM in the United States are obese.[1]

The distribution of body fat appears to be an even more important determinant in the development of diabetes and cardiovascular disease than the total amount of fat. Fat stored in the upper body (android) is associated with greater risk than fat stored in the lower body (gynecoid).[2,3] Men typically store fat in the upper body (abdomen) and women tend to store fat in the lower body (hips and thighs). Individuals with android obesity have higher insulin levels, fasting blood sugar, and triglyceride levels, as well as blood pressure, compared to persons with gynecoid obesity.[3,4] Individuals with android obesity tend to have larger and more metabolically active fat cells, and thus may have an easier time losing weight than those with gynecoid obesity.[5] Although gynecoid obesity carries a lower medical risk, it is weight that is more difficult to lose.

Obesity may be due to multiple causes, including heredity, altered metabolism, excessive caloric consumption, and reduced physical activity. Whatever the reasons, when energy input is greater than energy expenditure excess fat is stored. Although the mechanisms are not understood, obesity leads to an impairment in insulin action or insulin resistance. In nondiabetic persons the pancreas is able to compensate for the development of insulin resistance by increasing the secretion of insulin. Patients with NIDDM have a dual defect—more severe insulin resistance and an impairment in insulin secretion.

It is well known that weight reduction improves glucose tolerance and decreases risk factors for coronary heart disease (CHD) in obese individuals with NIDDM. Even modest weight loss (10 to 20 pounds) can improve blood glucose levels and insulin sensitivity, resulting in reduction of the need for oral hypoglycemic agents or insulin doses.[6] Blood glucose response to weight loss appears to be most effective in patients with short duration of diabetes.[7] However, one study noted that duration of disease had no effect on blood glucose levels after weight loss.[8] The degree of obesity or the rate of weight loss appears to be unrelated to improvement in blood glucose levels.[9] Individual response to weight loss varies, but blood glucose levels are usually maximally reduced within two weeks after the initiation of caloric restriction even though weight continues to drop.[6,10] Reduction of caloric intake below usual levels, rather than weight loss itself, affects glycemic control. Glucose levels after five to 10 pounds of weight loss predict glucose levels after 20 pounds of weight loss. These changes appear to be due to improved peripheral insulin sensitivity, decreased hepatic glucose output, and enhanced ß-cell activity.

Defining Obesity

Before implementing strategies for effective weight loss, it is important to determine the extent of the patient's obesity, and thus assess the level of risk and determine the course of action. Evaluating body fat directly is not possible and so indirect methods are used. Hydrostatic weighing to determine body density is the gold standard. Skinfold fat measurement using calipers is useful, but it is dependent upon the assumption that the selected sites reflect the average thickness of the entire subcutaneous fat mantle. Computed tomography, magnetic resonance imaging, bioelectric impedance, and total body electric conductivity are sophisticated techniques to measure body fat, but are expensive and not appropriate for clinical practice.

One convenient measure that can be used to establish the degree of obesity is relative weight, or weight in relation to height. Frequently standard height/weight

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tables, such as the Metropolitan Life Insurance Tables, or formulas such as the rule of thumb method (see Table 1 of article by Wylie-Rosett and Engel in this issue) are used to compare individuals to the population. Twenty to 40% above DBW is considered mildly obese and an established health risk.[11,12] Forty-one to 100% above DBW is termed moderately obese, and more than 100% above DBW is judged to be severely obese.

Body mass index (BMI) is useful in determining the degree of obesity and is highly correlated with body fat as estimated from body density. BMI is calculated by dividing weight in kilograms by height in meters squared (kg/m^2). A BMI greater than 27 corresponds to a body weight of 20% or more above DWB and is indicative of obesity[11] Although the BMI is helpful in evaluating degree of obesity, it is difficult to translate its meaning to patients in terms of the amount of weight they need to lose. The waist/hip ratio (WHR) is a valuable measure to determine body fat distribution and predict metabolic alterations. A WHR greater than .85 is associated with android obesity and places individuals at greater health risk.[13] The WHR may be measured slightly differently by various individuals. Generally, it is assessed by measuring the circumference of the minimal waist and the maximal hip girth in the standing position.

Assessment

Before beginning any weight loss program a nutrition assessment must be obtained. In addition to current dietary habits, questions regarding weight history, dieting history, family and social support system, financial concerns, and exercise patterns are crucial. Most importantly the level of motivation must be assessed.

Brownell has proposed the concept of readiness and has developed an assessment tool to evaluate it.[14] He emphasizes the importance of determining a patient's readiness by looking at goals and attitudes, hunger and eating cues, control over eating, binge eating, emotional eating, and exercise patterns and attitudes. Determining the degree of readiness can either identify specific areas of weakness that patients can improve on, or help assist an individual in realizing that it is not the right time to start a diet and risk possible failure.

Weight Loss Options

Components of a successful weight management program should include nutrition education, behavior modification, exercise, and group or individual support. Significant weight reduction takes a long time to achieve and staff are needed to provide the continued education and support. Because of personnel and time required to achieve success, many physicians find it difficult to plan and manage weight loss programs in their offices. One option is to refer patients to a registered dietitian in private practice or a local hospital outpatient nutrition clinic for one-on-one counseling. Alternatively, one can create a multidisciplinary team in one's practice and collaborate with a registered dietitian.

Conventional low calorie balanced diets incorporating education, behavior modification techniques, exercise, and follow-up support are widely accepted among health professionals. There are a number of regimens which fit this description. The exchange system (American Diabetes Association and American Dietetic Association) is familiar to many patients with diabetes. These diets are intended to produce gradual weight loss. Meal plans are developed by registered dietitians in an individualized manner based on lifestyle and typical eating patterns. However, only highly motivated, intelligent patients seem to feel comfortable using it.

The exchange system is often viewed as too complicated and too structured for many patients. Some prefer simply to count calories. Many food labels list calories per serving, and there are numerous books available that list energy values of commonly used foods. This method is appropriate for patients treated with diet alone or with hypoglycemic agents; it may be used cautiously with patients taking insulin. One concern with calorie counting is that dieters may select a nutritionally inadequate and unbalanced diet. However, Wing et al showed that most patients who use calorie counting select a diet that is nutritionally adequate.[15] A more simplified approach can be used with patients who have limited intellectual abilities. Specific goals for behavior change are developed based on the diet history. There has been some success in those who limit only their fat intake.[16] Some insulin-treated diabetics count only carbohydrates or calculate total available glucose (TAG system) to match insulin doses. However, these methods are not as appropriate for obese patients, since they are not designed for weight reduction.

An alternative approach is group weight-loss programs. Weight Watchers uses a diet similar to the exchange system and emphasizes group support as well as nutrition education, exercise, and behavior modification. Other private organizations that provide group support include TOPS (Take off pounds sensibly) and Over-eaters Anonymous.

Some low-calorie balanced diet programs require the purchase of prepackaged foods. This provides the convenience of eliminating food selection and meal preparation, factors that make these programs particularly attractive to single patients who live alone. However, the apparent advantage of convenience may also be a disadvantage in the long run. Patients may not receive adequate nutrition education or practice in making proper food choices.

Since weight loss is relatively slow (goal of one or two pounds/week) with traditional diets, many obese Type II diabetics may benefit from a more intense approach producing a rapid weight loss. Very low calorie diets (VLCD) in the form of regular food (protein-sparing modified fast) or liquid supplements provide between 400-800 calories. Today's liquid diets differ from those used two decades ago which were sometimes associated with death due to cardiac arrythmia. Present formulations contain sufficient amounts of high biological value protein as well as vitamins, minerals, and adequate fluid, and are considered relatively safe when medically supervised. Psychological benefits result from rapid initial weight loss and provide incentive to continue.[17] This weight loss can markedly improve complications of obesity and diabetes by reducing blood glucose, insulin and cholesterol levels as well as blood pressure levels.[18] VLCD's are an acceptable alternative to conventional therapy when used appropriately in conjunction with a behavior modification and exercise program.

The risks of VLCD are increased when used without medical supervision, when consumed by individuals who are not severely overweight, and when prescribed by physicians untrained in their use.[19] Short-term complications may result from the inappropriate use of the supplements or by consuming less than 800 calories/day of conventional foods. Symptoms may include dehydration, electrolyte imbalance, orthostatic hypotension, and increased uric acid concentration. Long-term complications include the risk of severe ventricular arrhythmias, cholecystitis, and pancreatitis during the refeeding period. The mildly obese lose more lean body mass (LBM) on a hypocaloric diet than the morbidly obese. Additionally, large losses of LBM decrease the resting metabolic rate and may reduce lean mass below normal limits, making it more difficult to maintain desirable weight.

It is important to screen potential patients before making recommendations to join a VLCD program. Absolute contraindications are malignant arrhythmias, unstable angina, protein-wasting disease, major organ failure, drug therapy that can cause protein wasting (ie, steroids, antineoplastic agents), and body weight less than 20% above DBW or a BMI of less than 25. Relative contraindications are congestive heart failure, drug therapy with potassium-wasting diuretics and adrenergic stimulating agents, history of failure to comply with medical regimens, and body weight less than 30% over DBW or a BMI of less than 30. Caution should be used in individuals with angina or a history of heart disease, the presence of a systemic disease, a history of psychiatric or emotional disorder, and chronic drug therapy including insulin.[17] Although it is not recommended for patients taking insulin, when doses are carefully titrated and blood glucose levels monitored closely VLCDs have been safely used. Sometimes physicians prescribe a VLCD using liquid supplements or frozen entrees for one to three meals a day in an effort to limit food selection and preparation and maintain calories at 800 to 1000/day. These may be recommended in frustration because of a patient's failure or poor outcome with previous diet attempts. However, because typically there is no education in behavioral changes or nutrition to accompany the prescription, long-term success is limited. There are no data published, however, on the success of weight-loss diets administered through physician's offices. VLCDs in conjunction with behavior modification have been shown to produce greater weight losses than VLCDs alone.[20] The need for a multidisciplinary approach is essential. Frequent sessions (often weekly) for support, instruction in eating behavior modifications, and exercise should be included in a program.

Caution should be used when considering fad or novelty diets in which weight loss is achieved by macronutrient restriction or by using rigid rules of combining food. For example, the Beverly Hills Diet is deficient in protein, and Fit for Life claims that the metabolism of certain combinations of foods causes weight gain. Some diets such as the Scarsdale, Atkins, and Stillman diets are low in carbohydrates in order to promote ketosis to accelerate fat mobilization and produce rapid weight loss. These diets often do not meet the recommended dietary allowances (RDA) because they exclude major food groups. They are by nature boring and typically dieters adhere to them for only a short time, limiting the potential harm. Fad diets may have a deleterious effect on blood glucose levels and, because of the minimal success achieved, they can further the cycle of chronic dieting.

There is increasing evidence that frequent episodes of weight loss and regaining may predispose one to obesity. Animal studies indicate that with successive periods of gain, the efficiency of fat storage improves and weight gain becomes easier.[21] In Keys' classic feeding studies,[22] he reported that humans who were semistarved and then refed deposited a greater amount of fat and less LBM than previously. The body may be interpreting a hypocaloric diet as starvation and it adapts by decreasing the resting metabolic rate in an effort to resist further loss of fat stores. Each time weight is lost, the proportion of fat to LBM is increased. Since fat tissue is less metabolically active, less energy is then required for weight maintenance. Although further clinical research is needed, repeated cycles of weight loss and regain appear to be harmful and attempts should be made to avoid them.

Benefits of Exercise

Exercise and increased physical activity should be an integral part of any weight control program. By increasing energy expenditure in conjunction with reducing intake, a greater weight loss is produced than either therapy alone.[23] However, the benefits of exercise go beyond the number of extra calories utilized during the activity. Exercise helps offset the fall in the resting metabolic rate that is usually observed when weight loss is achieved solely by dieting. When exercise is added to a hypocaloric diet, lean body mass is preserved and fat mass is selectively reduced.[24] Exercise may also favorably influence cardiovascular risk factors[25] and offers psychological benefits which are often overlooked. Exercise can provide a sense of accomplishment and confidence and improve a patient's self-image.

Although exercise programs are often viewed pessimistically because of high attrition rates,[26] patients who continue to exercise have more sustained weight loss after one year than with diet alone.[27] Because of physical limitations and difficulties patients may have in committing to a formal exercise program, it may be more effective to incorporate increased activity into everyday living. Walking is appropriate for the morbidity obese patient. Frequency and duration suggestions vary from three to seven day per week and from 15-45 minutes per session.

Weight Maintenance

The maintenance of weight loss is critical, but is frequently the most frustrating and discouraging part of a weight control program. Although many patients lose weight, few are able to keep the weight off. In contrast to the maintenance phase of weight loss, initial weight reduction offers more tangible rewards for the patient's efforts. At first, there are immediate short-term weight reduction goals: a relatively large amount of weight is lost; contact with food is minimized; family and peer support is high; and exercise results in benefits of improved fitness and sense of well-being. In contrast, weight maintenance is life-long and on-going; the goal is to keep from gaining weight; patients must maintain constant vigilance over food intake; family support tends to diminish with time; and physical exercise must be continued to have a positive effect.

Strategies that patients can incorporate into their lives are critically important if weight loss is to be maintained. There are a number of behavior modification techniques that have been employed in weight maintenance programs. Self-monitoring of food intake, exercise, and mood appears to be effective in producing sustained weight loss.[28] Patients can develop a list of enjoyable activities that do not involve food in an effort to substitute nonfood-related activities and take the attention off food. The consequences of new eating behavior can be modified by developing immediate reinforcers for the new eating patterns; these include praise for positive changes and tangible rewards from family and friends. Another strategy is to eliminate cues that lead to inappropriate eating behavior. These include designating one room in the house in which all eating is done, changing the usual eating place at the table, avoiding eating while involved in other activities, removing food from all places except appropriate storage areas in the kitchen, leaving serving containers off the table while eating, never accepting any food unless it is asked for, and putting away ingredients before eating a prepared food.[29]

Negative thinking and social events can serve as cues for overeating. Patients need to learn how to manage these "high-risk" situations. They can be taught coping skills to deal with difficult periods. They must learn that they will inevitably have temporary lapses but can learn to recover and prevent lapses from turning into relapses. Family members can learn how to be supportive of the patient's efforts; patients with greater social support appear to do better than those without support.

Obesity in IDDM

Obese patients with Type I diabetes are being seen more frequently. For the most part, treatment approaches are similar to those used with NIDDM. However, VLCDs should be undertaken with caution. Blood glucose monitoring by the patient is essential as calories are reduced in order to titrate insulin doses to avoid hypoglycemia. Failure to adjust insulin doses may result in minimal weight loss because of frequent episodes of hypoglycemia with consequent overeating.

Conclusion

Noninsulin dependent diabetes is associated with obesity, an android distribution of body fat, and impaired carbohydrate and lipid metabolism. Weight reduction improves the metabolic derangements of NIDDM. After assessment of obesity and readiness, an appropriate diet program is chosen. Low-calorie balanced diets promote a slow, gradual weight loss and should be an integral part of a comprehensive weight control program, which includes education in behavior modification and follow-up support. Alternatively, VLCD therapy with a behavioral component, may be appropriate for some patients and offers advantages to the obese person with diabetes.

Weight loss regimens are available in various formats, such as group or individual, calorie-focused or macronutrient-focused. The program chosen depends on an individual's motivation, education, and preferred style of learning. Financial status must also be considered since some programs are costly.

Diets that produce only partial success can promote weight cycling and this may make it more difficult to lose weight in the future. Maintenance of weight loss continues to be a difficult problem for the obese dieter, although there are a number of behaviors that will promote successful maintainance of weight loss.

Although it is desirable to reduce weight to DBW, this may not be necessary to improve glycemic control and lipid levels. A realistic attitude may reduce the pressure and decrease the frustration for both patient and physician. A modest weight loss accompanied by exercise can improve body composition and self-image, as well as diabetes control.

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The Diabetes Health Care Team: Spotlight on the Nurse Educator

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PATIENT education has long been recognized as an important component of quality diabetes care. Numerous studies have demonstrated that the self-management skills developed by participation in an outpatient diabetes education program decrease hospitalizations and thereby reduce medical costs in this population of patients.[1-6]

Diabetes education is a complex and dynamic process. Effective patient education requires planning, implementation, documentation, and evaluation. Adjustment to diabetes and to the demands of the treatment regimen is continuous throughout life. Diabetes and its complications can affect an individual's personal development, self-care behavior, social relationships, financial security, and choice of occupation. Therefore, ongoing education and counseling are necessary to foster acceptance and maximize adherence to the treatment program.

The major goals of patient education are; 1) to provide knowledge and skills; 2) to assist the patients and their families in adjusting to the psychological and social demands of living with a chronic disease and; 3) to help patients and families make and sustain the necessary lifestyle modifications.

Patient education and counseling are equally important for individuals with Type II and Type I diabetes. Traditionally, Type I diabetes has been viewed as being more serious; however, it is now well recognized that individuals with Type II diabetes are also at risk for increased mortality and morbidity, and will benefit from teaching. The educational program should be individualized for each patient, taking into account the individual's specific needs and resources. Initial teaching sessions will focus on "survival level skills and information," ie,

- insulin injection technique
- basic nutrition principles
- glucose monitoring
- prevention and treatment of hypo- and hyperglycemia.

Over time, more in-depth and ongoing counseling is needed to maximize quality of life and promote independence and positive self-care behaviors.[7]

This type of comprehensive diabetes care is best provided by a health care team. Within the team concept, patients and health care providers work together to provide quality care. A team most often consists of a patient, physician, nurse educator, and nutritionist. Other health care providers such as an ophthalmologist, podiatrist, or social worker may be needed at various times during the course of the disease. Although ideal, a complete team may not be realizable in a private office or small clinic.

However, with the increasing numbers and availability of diabetes education programs and nurse educators, these services are available to most physicians and patients on a consultation basis throughout the state.

The use of a diabetes educator and/or patient education program benefits both patient and physician. The team approach is both efficient and cost effective and it offers different perspectives on patient management. A well educated patient is better able to adhere to the treatment regimen and physician time is saved and the patient benefits by receiving more comprehensive care.

Most hospitals in Connecticut offer the services of a diabetes nurse and/or a diabetes education program. The diabetes nurse might hold one of a variety of titles such as diabetes educator (this title is also used by other health professionals such as registered dietitians, pharmacists, and physicians who are involved with diabetes patient

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education) or diabetes teaching nurse. The title diabetes nurse clinician or diabetes nurse specialist can also be used and usually denotes an advanced degree or specialized study in the area of diabetes management and education. Regardless of title. the diabetes nurse educator is skilled in both the teaching and learning process as well as in basic diabetes knowledge and management.

Beginning in 1985. diabetes nurse educators as well as other health care providers could be certified in the specialty of diabetes education. In September of that year. the National Certification Board for Diabetes Educators was established by the American Association of Diabetes Educators. Its purpose is to promote competency in diabetes education by providing voluntary certification by examination for all health care professionals involved in diabetes patient education.

To sit for the examination individuals must hold a current license or registration as an RN. RD. RPh. MT. PA. MD. or DPM. Other health professionals must hold a Master's degree in their specialty. To qualify. 2.000 hours of experience in diabetes education are required. The individual must meet all eligibility criteria and pass the examination to become certified. Certification is valid for five years. The American Association of Diabetes Educators as well as the State Chapter. Connecticut Association of Diabetes Educators. has a list of all certified diabetes educators in the state.

While certification denotes an acceptable level of expertise for the individual educator. the Recognition Process identifies quality diabetes education programs. In 1984 the National Diabetes Advisory Board in collaboration with many diabetes experts and agencies developed national standards for diabetes education programs. These standards consist of 10 components which include:

- Needs Assessment
- Planning
- Program Management
- Communication/Coordination
- Patient Access to Teaching
- Content/Curriculum
- Instructor
- Follow-up
- Evaluation
- Documentation

Their purpose is to improve and maintain the quality. effectiveness. and availability of diabetes education programs. The American Diabetes Association has assumed responsibility for the implementation of these standards. Centers applying for recognition have their programs reviewed and evaluated against the national standards. To date more than 270 programs have submitted applications to receive recognition status and 152 programs from 41 states and the District of Columbia have been recognized by the ADA.[8] This includes two programs in Connecticut—the Diabetes Life Care Program at Hartford Hospital and the Diabetes Care Center at St. Francis Hospital.

The inconsistency of third party reimbursement for diabetes education programs has limited access to education for many individuals with diabetes. In 1984 the ADA published a position statement supporting and encouraging adequate reimbursement and payment for outpatient diabetes education services. Although the number of reimbursable programs has grown from 154 in 1986 to 302 in 1989. reimbursement is by no means universal either throughout our state or the country. In Connecticut some outpatient education programs are reimbursed by Medicaid. Medicare. Blue Cross/Blue Shield. and private companies[9] and other institutions offer these services free of charge or on a sliding scale basis.

In summary. physicians are encouraged to choose an expert diabetes nurse and/or outpatient education program to assist in their management of the patient with diabetes. The certification and recognition processes can help the physician to identify high quality resources. Diabetes education can dramatically improve the quality of care we provide to patients with diabetes in the state of Connecticut.

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Chronic Complications of Diabetes Mellitus: Practical Issues for Primary Care Providers

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THE American Diabetes Association (ADA) has estimated that approximately 85% of the care given to patients with diabetes in the United States is provided by family practitioners and internists. This article on some of the chronic complications of diabetes mellitus is intended to highlight issues of clinical relevance to primary care providers; it cannot, however, be exhaustive in cataloging the complications of diabetes or in outlining pathophysiology and treatment. Rather, the intention is to review some critical issues and outline recommendations for daily office management of patients with both Type I and Type II diabetes mellitus.

The early manifestations of the chronic complications of diabetes mellitus present with no symptoms and are generally clinically silent. Therefore, it is up to the primary care physician to know what these complications are and how to screen for them in order to begin appropriate and timely therapy.

Ocular Complications: Diabetic Retinopathy

Eye complications due to diabetes mellitus are the leading cause of new cases of legal blindness (visual acuity of less than 20/200) in adults less than 65 years old in the United States. This represents approximately 6,000 new cases per year.[1,2] Most of this visual loss is due to macular edema and/or ischemia and vitreous hemorrhage with or without retinal detachment. Using a hand-held ophthalmoscope, most primary care physicians and many ophthalmologists can detect only approximately 50% of significant ocular lesions present. One of the most common lesions easily missed is macular edema. The American Diabetes Association position statement on eye care for patients with diabetes states, "People between twelve and thirty years of age with the diagnosis of diabetes mellitus of at least five years duration should have a baseline ophthalmic examination...."[3] The American Academy of Ophthalmology (AAO) has more formal guidelines for management of patients with diabetes mellitus based on their level of retinopathy.[4] These recommendations suggest baseline examinations for all patients with diabetes. The frequency of follow-up examinations varies from every six to 12 months for those patients with no or minimal nonproliferative retinopathy, to follow-up every one to two months for patients with high-risk proliferative retinopathy.

The specific recommendations of the ADA and the AAO, though not formally the same, are concordant and based upon the known epidemiology of eye disease in patients with diabetes mellitus. The clinical onset of Type I diabetes can generally be dated to within several months. Type II diabetes mellitus, on the other hand, begins insidiously and the patient may have impaired glucose tolerance or mild Type II diabetes mellitus for many years before the diagnosis is formally made by a physician. This issue of timing of diagnosis affects the recognition and management of complications in all patients with Type II diabetes mellitus, and this problem is growing. At the recent 51st Annual Scientific Sessions of the American Diabetes Association in Washington, D.C., in June 1991, new statistics revealed that there are probably some six to seven million undiagnosed patients with Type II diabetes mellitus in the United States.

The incidence of background (microaneurysms, intraretinal hemorrhage, hard exudates, and edema) diabetic retinopathy is approximately 20% in patients with Type II diabetes mellitus at the time of diagnosis.[1] In contrast there is a very small incidence of background diabetic retinopathy in patients with Type I diabetes mellitus at the time of diagnosis. Diabetic retinopathy of any type is rare in the prepubertal years. To contrast Type I and Type II diabetes mellitus, 56% of the former versus 24% of the latter will develop proliferative retinopathy

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(neovascularization of the optic nerve or extraretinal neovascularization) by approximately 20 years of disease duration. However, 10% of patients with Type II diabetes mellitus develop macular edema during the first 10 years of disease, while only 0.5% of patients with Type I diabetes mellitus will develop macular edema.[5,6]

There are several clinical factors that both primary care physicians and ophthalmologists need to be aware of in order to provide appropriate care. The amount and severity of diabetic eye disease is loosely correlated with disease duration and possibly with overall glycemic control. Thus patients seen for the first time whose disease is of a long duration or who have had poor glycemic control should be referred for complete baseline eye examinations. A sudden change in vision in a patient with diabetes mellitus may represent vitreous hemorrhage, retinal artery or vein occlusion, retinal detachment, neovascular glaucoma, or merely large swings in blood glucose levels. After office examination including fundoscopy, all of these patients should be referred to the ophthalmologist for further evaluation. From the reverse viewpoint, if the ophthalmologist observes a rapid change in retinal findings, this should prompt referral back to the primary care physician to reevaluate blood pressure and renal function; changes in either of these can rapidly accelerate the progression of disease. During pregnancy and growth spurts, diabetes mellitus should be carefully monitored, as retinal changes may accelerate. Lastly, if the primary care physician is attempting to improve overall glycemic control by changing from oral hypoglycemic agents to insulin, or from one injection per day to a multiple daily injection regimen, or from standard split-mixed insulin therapy to continuous subcutaneous insulin infusion, he should inform the ophthalmologist of this change in treatment plan. Both the Kroc and Steno studies revealed that in the short term (six-12 months) there is actually worsening of background diabetic retinopathy in patients on intensified insulin regimens; however, by two or three years following the initiation of the intensified insulin control, the study groups under better glycemic control were found to have fewer eye changes and less progression of retinal disease.[7,8] The etiology of this short term deterioration remains uncertain.

A recent cautionary note is that postpubescent children with Type I diabetes mellitus were found to have a greater prevalence of diabetic retinopathy than prepubertal children with similar duration of diabetes mellitus and perhaps should be treated as adults in terms of follow-up.[9] In terms of treatment, prevention remains the key issue, as both of the Early Treatment Diabetic Retinopathy Study reports show that later photocoagulation is effective in preventing deterioration of visual acuity from significant macular edema.[10]

Recommendations—

1. Educate your patients. Make them aware of the possibility of ocular complications and the necessity for routine eye examinations.
2. Perform ophthalmoscopic examinations on all patients with diabetes mellitus four times per year at their regular office visits.
3. Refer to ophthalmologists as noted above for baseline and follow-up examinations.
4. Keep the ophthalmologist informed of pertinent clinical issues, ie, pregnancy, puberty, changes in glycemic control, blood pressure control, renal function, and other concurrent medical illnesses.

Renal Complication: Diabetic Nephropathy

Diabetes mellitus is probably the leading cause of end-stage renal disease in the United States and accounts for 25-30% of new patients on chronic dialysis.[11] This represents approximately 4,000 new cases per year.[12] This is a major cause of morbidity and mortality in patients with diabetes mellitus.

The progression of subclinical to overt nephropathy appears to differ slighty in Type I from that in Type II diabetes mellitus. The initial changes in Type I diabetes mellitus of increased glomerular size and glomerular filtration rate are not seen in patients with Type II diabetes mellitus; however, once overt proteinuria has been established, the pathophysiology, disease progression, and response to treatment appears to be similar in both Type I and Type II diabetes mellitus. In Type I, overt proteinuria (urine dipstick positive equivalent to greater than 250 mg of protein excretion per day) in the first five to seven years after diagnosis is unusual, whereas 10-20% of patients with Type II diabetes mellitus may have proteinuria within the first five years after diagnosis.[13] Again, patients seen in the prepubertal years appear to be protected. These comparisons are inherently prejudiced by the difficulty in knowing the exact timing of the diagnosis in patients with Type II diabetes mellitus thus making the head-to-head comparison between Type I and Type II diabetes inherently biased towards the detection of more complications earlier because of longer disease duration in patients with Type II diabetes mellitus. Approximately 25-35% of patients with Type I diabetes mellitus develop overt proteinuria within 15-20 years of the onset of disease, while the number is approximately 50% for patients with Type II diabetes mellitus. Hypertension usually accompanies nephropathy seen in Type I diabetes mellitus, while hypertension is often a concomitant condition in patients with Type II diabetes mellitus. We now know that this is probably due to the pathophysiology of Type II diabetes which involves insulin resistance and hyperinsulinemia.[14]

Potentially one of the most important additions to our armamentarium against nephropathy is the ability easily to detect microalbuminuria (albumin excretion rates of 26-250 mg/day[15]). This amount of albumin is not detected by the usual urine dipstick methods. Multiple studies have demonstrated that microalbuminuria is a marker for increased risk of development of overt proteinuria and nephropathy in patients with Type I diabetes mellitus [15-17] and for the development of clinical proteinuria and an increased risk of death in patients with Type II diabetes mellitus.[18,19] Exercise, position, and other factors can affect protein excretion and the debate continues on how and when it is best to screen patients for microalbuminuria.

How should these epidemiologic issues and our ability to detect microalbuminuria affect the usual office care given by primary care physicians? As is the trend in all areas of medicine, the primary care physicians should focus on risk factors. Patients with diabetes mellitus with the greatest risk for development of diabetic nephropathy include those with a family history of hypertension and/or nephropathy, poor glycemic control, and those with other risk factors for the development of renal disease. As with most complications of diabetes, the issue of glycemic control remains controversial. Several studies have shown reversal of microalbuminuria with continuous subcutaneous insulin infusions.[20] This approach has failed in patients with overt nephropathy.[21] Aggressive therapy of hypertension appears to be our best weapon against the development and progression of diabetic nephropathy. Many studies have shown that antihypertensive therapy can slow the progression of diabetic nephropathy.[22] Most diabetologists agree that blood pressures of 140/90 mm of Hg are too high and that, if clinically tolerated, a goal of 120/80 should be pursued, though there remains controversy on the optimal goal for blood pressure.[23] In addition, the antihypertensive therapy given to patients with diabetes should be different from that given to hypertensive patients without diabetes mellitus. The worldwide trend appears to be to use either calcium channel blockers, angiotensin converting enzyme inhibitors, or alpha blockers as first-line antihypertensive therapy, while avoiding the use of beta blockers and diuretics if clinically possible.[23] Decreasing dietary protein merits mention. Lowering protein intake to 0.6 g/kg body weight may help slow the decline in renal function in patients with nephropathy. However, this degree of dietary protein restriction is significant and it remains unclear if this is something that may be recommended practically for large numbers of patients with diabetes mellitus with or without overt nephropathy.

Recommendations—

1. Be alert to risk factors for renal dysfunction; family history of diabetes mellitus and/or nephropathy, concurrent hypertension and other compounding variables such as urinary tract infections, nephrotoxic medications, or exposure to contrast media.
2. Follow blood pressure carefully at each quarterly visit and aim to treat blood pressure aggressively if it is greater than 140/90 in a patient without microalbuminuria or if it is greater than 120/80 in a patient who has either microalbuminuria or overt proteinuria.
3. Screen all patients who are routine dipstick negative for proteinuria for microalbuminuria, as this appears to be a marker for early nephropathy.
4. Though less of an issue of screening and prevention, patients with overt nephropathy and a declining glomerular filtration rate (GFR) should receive aggressive therapy for hypertension and early referral to both registered dietitians and nephrologists so that appropriate dietary and medical recommendations can be made. Consideration of dietary protein restriction, phosphate binders, and other therapy should be considered when the GFR is in the range of 20-50 cc/minute.

Neurological Complications: Neuropathy

There are many forms of diabetic neuropathy ranging from the common "stocking-glove" or distal polyneuropathy, to radiculopathy, autonomic neuropathy, and cranial mononeuropathies. Review of the many clinical manifestations of diabetic neuropathy are far beyond the scope of this paper, but have been reviewed in many journal articles and textbooks.[24]

Half of the patients with long-term diabetes mellitus develop clinical neuropathies.[25] Despite its wide ranging clinical manifestations, most chronic forms of diabetic neuropathy appear to have a similar pathophysiology. The mechanism pieced together by many investigators over the past 15 years, and well summarized by Dr. Douglas Greene is worth mentioning because understanding the pathophysiology leads to an understanding of how certain therapies have been targeted. His hypothesis links hyperglycemia to an increase in activity of the polyol pathway, decreased tissue myoinositol levels with impaired phosphoinositide metabolism and a decrease in sodium dependent myoinositol uptake which completes and perpetuates this destructive cycle.[26] The observation that patients with forms of diabetes mellitus other than autoimmune Type I and insulin resistant Type II may also develop neuropathy supports the metabolic causation of neuropathy. Despite this fairly tight hypothesis, some patients with poorly controlled diabetes mellitus never develop diabetic neuropathy. Thus, other genetic susceptibilities and biochemical deficiencies may well exist.

Pirart's data[25] alluded to above revealed an initial prevalence of diabetic neuropathy of approximately 7.5%

at the time of diagnosis, which then increased to approximately 50% after 25 years of disease. He noted that patients with poor glycemic control had a higher prevalence of diabetic neuropathy. Similar trends were reported in another population based study.[27] Good epidemiologic data on autonomic neuropathy and cranial neuropathy do not exist.

For primary care physicians the most important issue concerning diabetic neuropathy is different from the issues surrounding retinopathy or nephropathy. Though it may seem obvious, the most important issue is to recognize the diabetic neuropathy. Patients with peripheral sensory polyneuropathy often have increased nocturnal symptoms of numbness and pain. Their numb feet are often misdiagnosed as being due to vascular causes and their lateral femoral cutaneous neuropathy is often incorrectly attributed to degenerative disc disease. Radiculopathy is often misdiagnosed as being musculoskeletal in nature and may even mimic other conditions such as cholecystitis. If properly diagnosed, these patients can begin to improve glycemic control sooner and be given appropriate symptomatic therapy, while avoiding other potentially harmful studies that may not be needed. Loss of proprioceptive capabilities causing a shift of weight distribution in the foot often leads to callus formation and increased weight bearing over the metatarsal heads, thus making the patient more prone to develop foot ulceration. If loss of proprioception is picked up by simple examination the primary care physician can make a referral to a podiatrist for fitting with orthotics and/or special shoes to prevent problems. A common misconception is that vascular disease is the main and usual cause of diabetic foot problems. However, foot problems usually represent a combination of both neuropathic and vascular problems and it is not common to see significant ulcerations on a vascular basis alone. Cranial mononeuropathies may be misdiagnosed as a stroke or other central nervous system event. Vague abdominal symptoms, nausea, or constipation are often misdiagnosed as a vast array of other gastrointestinal problems while the true nature of the autonomic gastrointestinal dysfunction is missed. Again, appropriate diagnosis allows the primary care provider to initiate proper symptomatic therapy and request referrals if needed.

The weight of retrospective and cross sectional data favors tightened glycemic control to treat diabetic neuropathy. Several trials are currently under way to assess in a prospective, randomized controlled fashion a relationship between tight glycemic control and improvement in diabetic neuropathy.

Aldose reductase inhibitors appear both to decrease symptoms and improve nerve conduction velocities. However, depending on the agent, significant side effects have been a problem.[31] Whether or not as they are currently formulated these medications will be approved remains unclear.

Other specific therapies for neuropathies remain difficult, especially those that attempt to alleviate symptoms of painful neuropathy. Antidepressants such as nortriptyline, amitriptyline, or imipramine may be helpful in small bedtime dosages.[32] Carbamazepine may help in a small number of patients. There are few objective data to support the use of phenytoin though it is commonly tried. Phenothiazines have been added to the antidepressant regimen when a less than optimal response has been obtained. Data on use of vitamins remain conflicting. Treatment of autonomic diabetic neuropathy is more complicated and must be tailored to the specific ailment.[33]

Recommendations—

1. Following an old clinical axiom, you must first think of the possibility of diabetic neuropathy before you can make the diagnosis and begin to treat it appropriately.
2. While making the diagnosis of a diabetic neuropathy, you must be sure to consider other etiologies, especially vitamin B12 deficiency, drug, alcohol, or heavy metal induced neuropathies.
3. Tight glycemic control remains the first line of defense.
4. Carefully look for loss of sensation, loss of proprioception, and anhidrosis in the feet of patients with diabetes mellitus. Take time to educate your patients about their sensory deficits to help prevent diabetic foot problems.
5. All patients with diabetic neuropathy involving the feet should be referred to a podiatrist for a baseline examination and probable ongoing foot care.
6. The presence of sensory neuropathy leading to a lack of symptoms of angina is one of the reasons for recommending exercise treadmill testing in all patients over 35 with diabetes mellitus, especially before beginning an exercise program.
7. Routine screening of nerve conduction velocities and electromyograms cannot be recommended because of the poor correlation between test results, clinical symptoms, and extent of disease.

The Diabetic Foot

Diabetes mellitus is the leading cause of nontraumatic amputation in the United States with a rate of one per 125 patients with diabetes mellitus less than 65 years old, and one out of 10 in patients greater than 65 years old.[34] The two major risk factors for diabetic foot lesions are neuropathy and ischemia. Neuropathy affects the foot in multiple ways: sensory polyneuropathy with decreased sensation leads to an insensitive foot, and thus major acute traumas may not be felt, or small recurrent traumas may not be realized; autonomic neuropathy may lead to a dry foot making the foot more susceptible to cracking and to infections; and, as previously noted, loss of proprioception leads to changes in weight bearing with resultant poorly distributed forces leading to callusing and ulceration. It has become clear over the past several decades that the concept of microangiopathy as the cause of diabetic foot lesions is incorrect. What has been found is that the combination of several types of neuropathy in association with large and medium vessel disease leads to improper weight bearing and resultant maldistribution of forces and pressure necrosis in a foot with already impaired circulation, thus increasing the potential for ulceration.

A group of foot experts convened by the National Diabetes Advisory Board was asked to make recommendations to improve foot care and prevent amputations. With all the sophisticated equipment available to quantitate blood flow, neuropathy, weight bearing, and other aspects of pathology of foot disease, they were unanimous in recommending that physicians around the country take off their patients' shoes and simply examine their patients' feet!

Thus, as with the other complications of diabetes, the major role of the primary care physician in the treatment of diabetic foot lesions is prevention.

Recommendations[35]—

1. Examine your patient's feet at every visit, especially and including between all toes and the posterior aspect of both heels. Observe your patient's gait as he walks down the hallway and into the examining room, and inspect his shoes.
2. Conduct a neurological and vascular examination at least once annually.
3. Educate your patient on proper foot hygiene, foot wear, how to avoid trauma, smoking cessation, and what to do if any problems arise.
4. Refer all patients with neuropathy to a podiatrist for evaluation, and carefully evaluate all patients in whom you suspect even mild vascular compromise.

This short review on specific aspects of the chronic complications of diabetes mellitus is intended to point out what primary care physicians can and should do to prevent the onset and progression of these dreaded complications. Space limitations do not allow a discussion of macrovascular disease. Suffice it to say that in addition to good glycemic control, aggressive therapy of hypertension and hyperlipidemia, smoking cessation, and weight management are even more critical in patients with diabetes mellitus than in those without diabetes because of their increased cardiovascular risks. It should be clear by now that diabetes mellitus is a model condition for the primary care physician to screen for and to treat problems by emphasizing prevention. Whether it is in the management of retinopathy, nephropathy, neuropathy, or the diabetic foot, the cornerstones of care remain patient education, history and physical examination, several simple screening tests and appropriate and timely referral, especially to ophthalmologists and podiatrists. With improved care by primary care physicians should be able to decrease dramatically the incidence of blindness, end-stage renal disease, and amputations despite a population that is growing older and developing a higher prevalence of diabetes mellitus.

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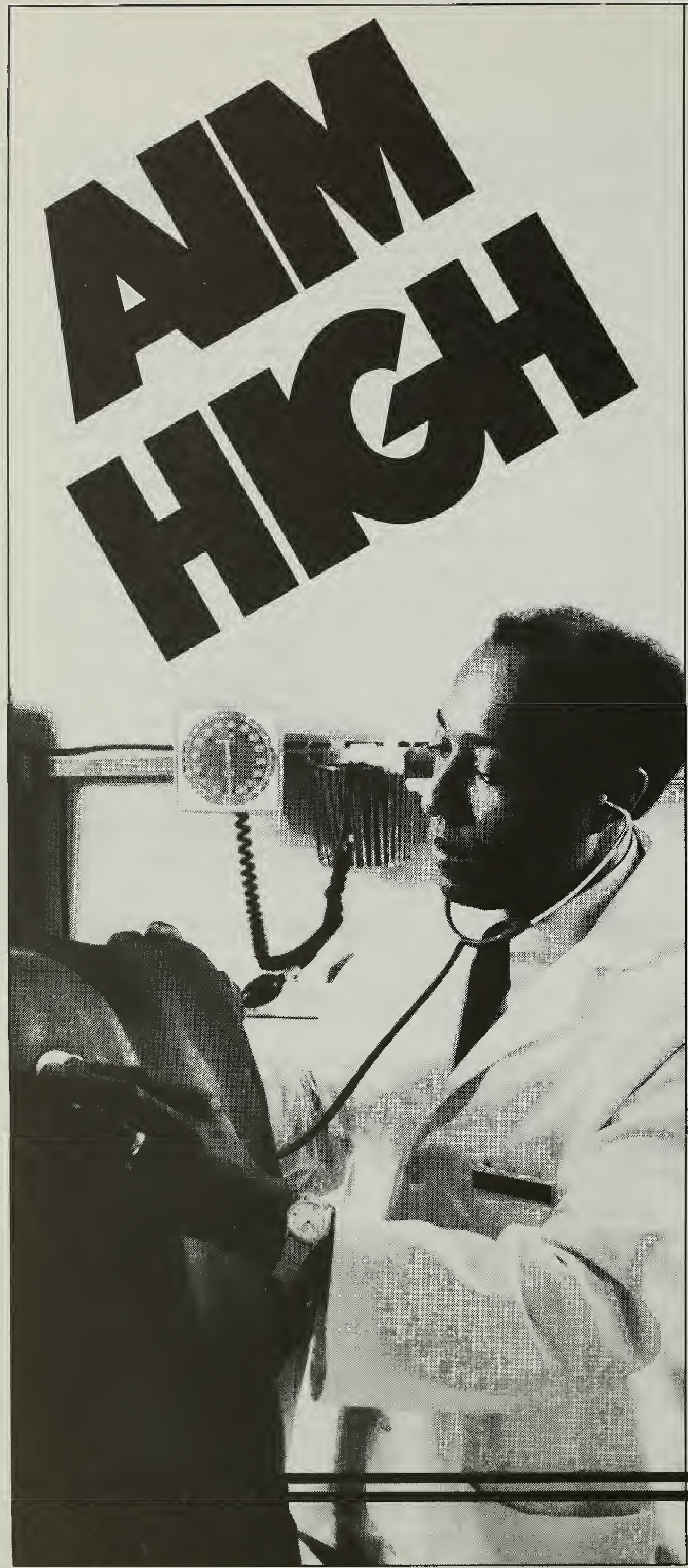

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HELPFUL HINTS

Time

E. TREMAIN BRADLEY, M.D.

TIME is scarce.
TIME flies.
TIME is infinite.

YOU can waste TIME. Or you can make TIME, but it better be with your spouse! More seriously—none of us seems to have enough TIME. Each of us will live a specific amount of TIME. Who knows what that amount is? So we want every hour, every minute to count.

TIME can be our master, a veritable slave-driver. No sooner do we start doing one thing than another demand crops up—and then another. Very distracting, confusing, disturbing. How do we handle it all? We want peace and satisfaction from what we do. My approach is, as each new demand arises, to assign a priority to each and give number one full unhurried attention without wasting TIME until it is complete or until another assumes priority number one. And so down the list: each item gets the full attention it deserves, and I'm not all frazzled when I attack the next.

Your 15-minute office appointment turns out to be more complicated and serious, lasts half an hour or more. That patient needs to be listened to, *with caring*, not feeling he is being hurried out the door. Unfortunately, others may have to wait. They can be assured that they will be afforded the TIME necessary for them. Some can even be delayed at home by phone to avoid a long wait.

Of course, it is predictable that some situations may need more TIME. Someone who has just lost a spouse, a beloved relative, a "significant other" needs to express grief, anger, fear, resentment, anxiety, frustration, dispair, whatever. It helps if we are sympatico, even sympathetic, yet retain some objectivity. And later on comes a lonely TIME, after the immediate blush of attention has faded. Arranging for family or friends to continue contact periodically is an aid to starting a new happy, healthy life.

A dying patient often needs support and the opportunity and TIME to air his feelings, which he may not be able, for whatever reason, to impart to his family or friends.

The unsung care-giver, cooped up with an infirm individual, is like the whale that has been submerged for a while. He then comes up for a breath of fresh air and "blows his stack." He needs TIME to talk and especially to have TIME away—temporary replacement being supplied, of course. Even an untrained person can come and read aloud, or play recorded music, or a book-on-tape. Result: peace for the care-giver and for the infirm, both.

Then there's the hurry call from the emergency room. Having excused yourself to the waiting patients, you hop in the car and whizz down the road. A slow-poke is in front of you. You ease across the center line and peer ahead: car coming. Retreat. Itchy and impatient, you keep on doing this, full of frustration until you finally get by and dash ahead, only to meet the next laggard. Elapsed TIME from office to ER is nine minutes. Or with a normal sense of urgency, you stay behind until a series of cars passes, you look, but no, not yet, with another car far beyond. Elapsed TIME is 11 minutes, but on arrival you are calm and have thought more about the emergency than about the traffic. TIME has not been your master; you have been master of TIME.

How about the TIME a visitor should spend with a sick patient? A big boost for the patient to have this attention, but it can be tiring. Even pleasant conversation can be exhausting. The patient feels, often unconsciously, the compulsion to be hospitable, to entertain the guest. So short visits are best, made frequently perhaps, with respites for the patient in between.

I remember an old man, with a wizened face, stooped, who might have been an athlete earlier on, but now well into his 80s. Oh no! he turned out to be only 49. How old is old, anyway? Should age be determined chronologically, by years, or physiologically? When is the "TIME to Retire (buy Fiske)," remember? After a certain number of months or years, or when the tires are worn down? Usefulness, capability, trustworthiness should be major criteria. The trouble is: who decides about people? Unfortunately personalities and the greed for power interfere. We want to keep active. The longer we live the faster TIME seems to fly by.

Why is it that when you want a good job done, you ask a busy person to do it? You know they are conscientious and have drive, but they really don't have TIME. Yet they make TIME. TIME is infinite.

E. TREMAIN BRADLEY, M.D., solo practice of general surgery, retired to Norfolk, CT.

Editorials

Guest Editorials

On Opposing the Use of the Pacifier

The other day I saw a young and attractive mother carrying her two-month old baby in a "Snugli," supporting the baby's bottom with one hand and holding a pacifier in its mouth with the other. Everywhere we go we see babies and young children sucking on pacifiers. Whether in the parent's arms, in a stroller, or even walking alone, many children—awake or asleep—are hooked on pacifiers. Apparently, we prefer our children to be silent in public and in private, particularly if they might cry. I think it is bad practice to offer an infant a pacifier at all. There are several good reasons to stop its use.

Crying is one of the few ways babies have to communicate with us about their needs. Crying is a signal, a way of alerting us to their discomfort, be it an earache, hunger, or fear. Crying alerts us to a child who is fretful, tired, bored, or craves attention from adults who are distracted by other activities. Occasionally, in breast-fed babies, the crying is caused by an insufficient supply of milk, and the pacifier can hide this fact.

Putting a pacifier in the mouth gives a clear message to that child to be quiet, that we are not concerned about what the child is feeling, and that we prefer silence. Would we use a pacifier if the child were laughing? Probably not; we dislike crying and find it annoying because we either do not know what to do about it or the crying is interfering with our pleasures or work. The pacifier is used for the comfort of the parent, not the benefit of the child. Would we tell an adult to stop crying and chew gum or have something to eat instead of trying to find out why there were tears?

Babies are seen, during ultrasound examinations, sucking their thumbs while still in the uterus, and we find it amusing and most acceptable. The thumb is nature's built-in "pacifier," under control of the child, and can be used as needed for the discomforts of teething, of anxiety, or of fatigue. Its value lies in its being controlled by the child, and not a technique learned by the child at the insistence of the parent. Babies tend to suck their thumbs for limited reasons such as teething or anxiety, and stop when these are not present. Of course, long-term thumbsucking would raise questions about long-term emotional issues needing to be addressed. The pacifier, like an ever-present bottle in crib, carriage, or walker, teaches the child that its concerns are unimportant to the parent at this moment.

Another important lesson learned by the child using a pacifier is that our problems—emotional or physical—can be solved by putting something is our mouths. "Don't cry, my dear; here is a cookie!" This can be the beginning of a most unfortunate series of events. If we are taught to handle our discomforts so early by putting a pacifier in our mouths, and then a cookie, we can see the lesson the child learns. Whenever we are unhappy or displeased, we should put something in our mouths: food, a cigarette, a drink. Our times of unhappiness or sadness can be eliminated this way. We teach our children to be quiet, and find relief from their immediate problems by oral gratification. The result may well be a long, losing battle with being overweight.

As our front teeth our coming in, they are kept in their proper vertical position by our closed lips. These teeth are easily moved outward by an ever-present pacifier, and we see the oval slot where the pacifier fits in many young children. This can cause permanent alteration in the shape of the mouth and the face unless the pacifier is abandoned before the second teeth appear.

We must be very careful about the early signals we send to our children. Is it better to be seen than heard, as we oldsters were told? Is the world around us of such little interest that our children should have to withdraw into providing the simple pleasures found in sucking on a nipple? It would seem to be in an infant's best interest that we try to find out the immediate cause of crying or fussing and correct that as best we can. Crying is a legitimate and acceptable response to what is happening, and needs to be attended to by caring parents.

Alan C. Mermann, M.D., M. Div.
Chaplain, Yale University School of Medicine

HIV Partner Notification in Connecticut

The CSMS House of Delegates Resolution

The Connecticut State Medical Society House of Delegates approved a resolution at the 1991 annual meeting which supports HIV/AIDS partner notification programs. It is important that the leaders of organized medicine in Connecticut are supportive of the program of the State Department of Health Services to counsel patients with HIV infection and assist them in notifying sex and needle sharing partners who may be at risk. However, the program will not succeed unless the Society membership as a whole supports and uses this program. The program has been in operation for over a year but is underutilized by physicians.

What Is Partner Notification?

For HIV, partner notification is the process whereby an HIV-infected individual is counseled and assisted in the notification of sex and needle sharing partners so that those partners will have the information they need to seek HIV counseling, diagnosis, and treatment. The HIV-infected patient should be counseled and educated by his or her physician (or designee) on how to notify partners. The process should begin during pretest counseling. The concept of notifying partners at risk should be introduced as a basic element of HIV pretest counseling.

Studies from other states have shown the utility and acceptability of partner notification as a component of comprehensive HIV prevention programs. Most partners are unaware of their level of HIV risk. They are highly appreciative of being counseled. The seroprevalence of the sex and needle sharing partners is high.

How Partner Notification Occurs

Partners of persons found to be HIV infected can be notified of their risk in different ways.

- The partners can be notified directly by the HIV-infected patient with or without the direct assistance of the physician.
- The partners can be notified and counseled by one of the highly trained public health outreach workers from the Connecticut Department of Health Services Companion Awareness Risk Education (CARE) Program.

Notification of Partners by the Physician

If the infected patient asks the physician to notify a third party, the physician may do so. The physician has two options: either to assist the patient in talking to his or her partners, or to notify the partners without the infected person present. In the latter case, the name of the infected person must not be used without permission. Of course, the name of the infected person may be inferred by the partner in some situations, but the physician should not assume so and must refuse to answer a partner's request for the name.

If the physician is aware that specific partners are at risk and that the infected patient will not notify them, the physician has the legal privilege (but not the duty) to ensure that the partner is notified. All persons who are tested for HIV infection should be advised before they consent to testing, that if they do not wish to notify partners at risk, the physician may notify partners or request that the State Department of Health Services CARE Program make the notification. The physician may directly notify a partner at risk only if that partner is also a patient of the physician.

Notification by Public Health Outreach Workers (The CARE Program)

The CARE Program staff may be called for advice or assistance at any point in the partner notification process. The CARE staff are highly trained outreach workers who can go into the field to notify partners at risk. The CARE program *must* be used for any notification of a partner without the permission of the infected person unless the partner is already a patient of the physician.

The CARE program has been in operation for the past year. Of the 28 HIV-infected persons referred to the CARE Program in 1990, 55 partners were identified, contacted, and counseled by the CARE Program. Twenty-eight of them consented to HIV testing. Twenty were seronegative and eight were seropositive. Connecticut also received 22 referrals from other state health departments. The majority of these partners were contacted,counseled, and consented to testing.

The CARE Program has received referrals from the State Correctional system, local health department HIV counseling and testing sites, and some of the major hospitals in Connecticut. The CARE Program did not receive any referrals from physicians in private practice in 1990. Physicians are encouraged to use the HIV partner notification CARE program routinely. This is a vital program in light of the public health importance of the HIV epidemic and the needs of the patients and their partners. There are many physicians in Connecticut with HIV infected patients who could benefit from these services.

Where to Call

The CARE program coordinator, Wanda Coleman Richardson, can be reached at 579-6974 or 566-4492, Monday through Friday 8:30 am to 4:30 pm.

Richard Melchreit, M.D.
Medical Associate, AIDS Section, State Health Department

50 Years Ago

From *The Connecticut State Medical Journal*

November 1941

Physical Status of American Young Men

G. St. J. Perrott, Washington, D.C.

The Author. M.A. *University of North Dakota, 1915. Chairman of the Health Division of the District of Columbia Council of Social Agencies, Chief Division of Public Health Methods, U.S. Public Health Service, National Institute of Health*

While death rates among young men, aged 20-34 years, have declined nearly 30 percent since the World War, results of Selective Service examinations show no improvement in the physical fitness of living young men. About 43 percent of all men examined are being declared unfit for general military service either by local draft boards or at army induction centers. This compares with a figure of about 30 percent rejections in 1917-1918. Among the important causes of rejection are defective teeth (8.3 percent of all men examined), eye defects (5.0 percent), heart diseases (3.7 percent), musculoskeletal defects (3.2 percent), nervous and mental diseases (3.0 percent), ear, nose, and throat diseases (2.4 percent), hernia (2.0 percent), respiratory diseases, largely tuberculosis (1.7 percent), venereal diseases (1.6 percent), foot defects (1.4 percent), underweight (1.4 percent).

Of the 43 percent of men declared unfit for general military service, 32 percent are so classified by the 6,450 local boards and an additional 11 percent at the Army induction centers. This means that out of every 100 men declared physically fit by the local boards, an average of 16 are rejected in the thorough re-examination at the Army induction centers.

While draft board and Army physicians rejected 43 percent of the men for full military service, only 28 percent were considered unfit for any service. The remaining 15 percent were classed as fit for limited service and many of these undoubtedly had defects which were remediable.

The most striking difference between the results of 1917-1918 and today is the present high percentage of rejections because of defective teeth which are over four times as high as the World War draft. It should not be concluded that this necessarily indicates an increase in the prevalence of dental disease since 1918. It may indicate that young men today have had less dental care during childhood and adolescence than those of 1918, due to perhaps to the effect of the depression. Furthermore, while army standards have not changed since the last war, it is possible that they are being more rigidly enforced today. Other factors may play a part, such as the fact that deferments because of dependents or essential occupation tend to concentrate young men of low economic status who have had inadequate dental care in the group who are certified for physical examinations.

Rejections for respiratory disease (largely tuberculosis) are only a little lower than in the World War (1.7 percent as compared with 2.0 percent). Since mortality from tuberculosis has been cut in half in that time, it would appear that a better case finding job is being done in the present examinations.

Rejections for venereal disease constitute 1.6 percent of men in the present examinations as compared with 0.5 percent in the last draft. This higher percentage need not indicated an increase in the prevalence of venereal disease and to the use of better diagnostic methods.

In spite of the higher percentage of rejections reported today than in 1917-1918, it can not be said that the physical status of young men has deteriorated since the World War. Neither can it be said that the health of young men has improved. Differences in physical examination standards, in technique of examining physicians, and other factors make comparison difficult until the data can be analyzed in more detail. Rejections for defective teeth are obviously higher in 1941 than in 1918; otherwise the important causes of rejection today are the same as those in the World War draft.

—Abstract of a paper presented at the *Clinical Congress of the Connecticut State Medical Society*, September 17, 1941

The Utilizers

Who are the utilizers of medical care in America and how can we divide them up so that we can examine each group from different points of view? The "who" is followed by the "why" and "what" they give and take from our health care system.

The Uninsured: Much has been said about these 33 million American citizens, the majority of whom work for small businesses which do not provide health insurance, or are "between jobs." To obtain coverage as an individual is very expensive because the insurance industry is regulated in each state, and the legislators in each state have seen fit to listen to small groups demanding that any health care insurance policy contain coverage for many different specific illnesses. This has resulted in many mandated coverages, wanted or not, being added to all health care policies, and has placed the cost beyond the average economic means. In the state of Connecticut we have 16 added mandates. This uninsured group tends to forget about preventive medicine and to concentrate on crisis treatment only, using emergency rooms, the most expensive form of medicine in America. Their bills are sometimes paid, but more often they are grossly discounted or written off.

The Underinsured: These are the people who have health insurance, but only on a minimal basis. The best known of these coverages are sponsored by the government such as Medicaid and Medicare. Some private insurance policies are so structured that some chronic diseases are not covered. The *Medicaid* program is for those whose income is below poverty level, and, for the most part, this group consists of less educated folks who tend to ignore prevention and to utilize the expensive forms of crisis medicine.

As a group, the biggest spenders of health care dollars are the over 65-year-olds, which is the *Medicare* group. It is important to remember that 85% of the monies spent on health care during one's lifetime is spent during one's final 24 months. The 65-year-olds have been given to believe that with Medicare A & B and the supplements, there are no other applicable fees involved for health care.

This is, in fact, a national health care system for the elderly. Once a person graduates from the private sector at 65, the feeling is that Medicare will pay for private medical care. Unfortunately this is not the case—Medicare fees are generally in the 50-60% range of the usual and customary fees of hospitals and physicians. As overhead at the office is also in the 50-60% range, one can easily see that most physicians lose money by seeing Medicare patients in their offices. Less than honest physicians can check their patients' hearts today and have them back tomorrow to check their lungs. I know that if I give my patient two injections instead of one than I would get twice the fee. This is not the way to practice medicine, but the powers that be, ie, the government, HMOs and managed care firms, have been making the rules by economic, not medical standards. The hospitals are equally as badly treated by Medicare, as Medicare only pays somewhere between 50-60% of the bill each year, and the rest has to be written off and passed on to the paying public and to the businesses who provide their workers with health insurance. The system, with its escalating costs and discontented patients, payers, and physicians, is a disaster for everyone.

The Uninsurable: This is the group of utilizers for whom we all should feel most sorry. These are the people who have chronic and/or ongoing problems which will not be covered in the future. People who lose or change jobs currently under COBRA can carry their old insurance policy for 18 months, but then they have to obtain a new policy which so often will exclude preexisting conditions and, of course, be very expensive. Today many of these policies will require an AIDS test. Can you imagine any of these insurance companies giving health insurance to a person with a positive test for HIV? Certainly if they did they would not be in business for long. This group of utilizers need our help the most, as they are behind the eight-ball with no escape.

US: The Workers of America: This group of utilizers who have a job and health insurance which is usually paid through our employers, and for the most part is tax deductible. This is a fact and different from all the other utilizers whose in insurance and payments are not tax deductible. We believe in preventive medicine and take care of minor problems before they become huge. We know that there are nine preventable chronic illnesses which account for over 50% of all deaths. We also pay our way, not only for ourselves, but through Social Security and taxes we pay for Medicare, Medicaid, and all the other utilizers. Yes the "US" group carries the whole system. We the workers of America pay for the physicians and all the providers, including the hospitals, drug companies, and the HMOs. We pay for the government's health care systems and for health insurance companies and their profits. As the percentage of workers to the total population gets smaller every year, those who are working shoulder a larger and larger burden. Our backs are bent and we cannot go on. The cost of the world's finest medical system cannot long be carried by so few.

Anthony P. Redmond, M.D.
President

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REFLECTIONS ON MEDICINE

Euthanasia

ROBERT U. MASSEY, M.D.

I will neither give a deadly drug to anybody if asked for it, nor will I make a suggestion to this effect. Hippocratic Oath.

"Were I of Caesar's Religion, I should be of his desires, and wish rather to go off at one blow, than to be sawed in pieces by the grating torture of a disease," wrote Thomas Browne, who, but a few lines before had written, "...but where life is more terrible than death, it is then the truest valour to try to live." And later, "He forgets that he can die who complains of misery; we are in the power of no calamity while death is in our own."[1]

The religious denunciation of suicide is not exclusively Judeo-Christian. The Pythagorean origin of much of the Oath has been argued by Ludwig Edelstein, especially the rules concerning abortion, suicide, and the giving of a deadly drug.[2] In *Phaedo* Plato quoted Socrates:

> There is a doctrine whispered in secret that man is a prisoner who has no right to open the door and run away; this is a great mystery which I do not quite understand. Yet I too believe that the gods are our guardians, and that we men are a possession of theirs...Then if we look at the matter thus, there may be reason in saying that a man should wait, and not take his own life until God summons him....[3]

St. Augustine left no doubt that in his view suicide was the worst of crimes. The mind of Christendom seemed to agree, for suicides were denied burial in hallowed ground; to make an example of them, they were often buried at the crossroads with a stake driven through their hearts. Our aversion to suicide runs deep, and as physicians we have been taught to regard it not as a rational act, but as the preventable outcome of a serious disease.

In November the citizens of Washington voted on a referendum that would permit physicians to do what the Oath condemns. Of course, there would be requirements that would have to be met to safeguard against any kind of indiscriminate use or misuse of this new power. Anyway, the rules in a 2,000 year old pagan oath whose origins are obscure, and that has already been broached in the matter of abortion must only be binding in a kind of traditional or ceremonial way. Furthermore, Jack Kavorkian has discovered that in Michigan there is no law against assisting in suicide.

When I have spoken with students and house staff about this matter, they, like Thomas Browne, have been of several minds: suicide may at times be rational, it always signifies depression, it is cowardly, it is against religion, perhaps a crime; but on one point they have been unanimous: doctors must not be given the power to take life. It is not because there may not be times when it would be merciful to accede to a patient's request, but that given a hundred such cases, we should never agree. In one way or another these young physicians felt the reality of a slippery slope, the ease with which the first offense against a deeply held tabu or conviction can be repeated, and then again and again, each time with less revulsion. It was deliberate killing they had in mind, not the giving of morphine to relieve intractable pain, even though death might be hastened. It was giving a lethal drug such as potassium chloride that could have no other effect than to stop the heart, or an overdose of a hypnotic drug far beyond that needed to control anxiety or pain, that would be inexcusable; in these instances no physician could plead "unintended effect."

In 1826 a medical student wrote his thesis, "Medical Euthanasia," by which he did not mean what is now meant by that term; *euthanasia* is a euphemism like "putting to sleep," or in the Washington terminology, "aid in dying." Its actual meaning is simply "a good death," and it was the student's assertion that the physician had an obligation to assure a *euthanasia* for his patient, "...and least of all should he be permitted, prompted either by other people's requests or by his own sense of mercy, to end the patient's pitiful condition by purposely and deliberately hastening death."[4]

Nothing has occurred to in 165 years since that medical student from Goettingen wrote his thesis that should prompt us to call him outdated.

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Malpractice Reform: The No-Fault Options

JOSEPH M. HEALEY, J.D.

OPPONENTS of the existing medical malpractice system are often proponents of an alternative that compensates harm without regard for the negligence of the physician. In a no-fault system, a class of harms is identified and compensation is provided when those harms occur within a doctor-patient relationship. An injured patient need not establish that the harm was directly and proximately caused by a breach of the duty owed by the doctor to the patient, as required under the present system. Such an alternative system could take one of two forms. In one, the no-fault approach is applied only to certain types of injuries. In the other, the no-fault approach is applied as a general replacement for our current fault-based system. In either case, many of the limitations of the current system would be addressed by changing drastically how liability is established.

The advantages of a no-fault system are clear. When patients are compensated for injuries occurring within the doctor-patient relationship without regard for the doctor's fault, resolution of claims can be made more quickly, with less expense, and hopefully, with greater likelihood that the injured party will recover for the injuries. The weaknesses are also straightforward. Under such a system, whatever deterrent effect and incentive to responsible behavior are created by fault-based liability would be limited or eliminated. Of greater concern has been the likelihood that under a no-fault system, the number of claimants entitled to recover would be larger than under the present system, cancelling any benefits from the reduced cost of the system. Supporters of a no-fault alternative had been discouraged by the implication of the earlier research[1] suggesting that the number of compensable events under a no-fault system would be so much larger than the number of events compensable under the existing system that savings would be cancelled out by increased distributions.

Research sponsored by the Robert Wood Johnson Foundation's Medical Malpractice Program provides some useful data to consider these questions in the context of partial and complete no-fault systems. The work of Tancredi and Bovbjerb[2] has examined a common form of selective no-fault program (an "Accelerated Compensable Event" [ACE] System) and the work of Brennan and his colleagues in the Harvard Medical Practice Study of New York hospital[3] has reconsidered the conclusions of Mills and others about the economic implications of a total no-fault option. This month's column will focus on the ACE system, while next month's will consider the conclusions of the Harvard Study.

An ACE system would divert certain cases from the existing malpractice system into a no-fault system resembling worker's compensation. The cases included would be those medically-caused injuries that are usually, though not invariably, avoidable through good medical care. An ACE system is grounded in the experience of medical care and in the study of what injuries occur and whether they are preventable. Tancredi and Bovbjerb have listed the three main criteria for identifying an adverse medical outcome as an ACE: (1) avoidability (medically caused, but moderately or highly preventable as a class); (2) detectability (each group is readily specified and easily identified); and (3) absence of bad incentive effects (avoids distorting medical decision making).[2(p150)] Non-ACE injuries would remain within the existing malpractice system and would be evaluated in the same manner as at present. In his presentation at the final annual meeting of the Robert Wood Johnson's Medical Malpractice Program, Dr. Tancredi reported that a study of closed obstetrical claims revealed that half of the events, two thirds of the permanent serious injuries, and three fourths of spending by the current system could be covered under an ACE system.[4(p4)] While some raise questions about the extent to which directing the "clear-cut" cases from the existing system would improve the overall system, others view the existence of such an alternative to be the first step toward reform. As Professor Abraham concluded:

> "What we need is further experimentation with very discrete, limited sets of compensable events that are carved out of the tort system for no-fault compensation. If they work out, and people are satisfied with them, then that can be the model for the future."[4(p5)]

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Letter to the Editor

Letters to the Editor are considered for publication (subject to editing and abridgment), provided that they are submitted in duplicate, signed by all authors, typewritten in double spacing, and do not exceed 1½ pages of text (excluding references). They should not duplicate similar material being submitted or published elsewhere. Letters referring to a recent *Journal* article should be received within six weeks of the article's publication.

REPRODUCTIVE DEATH?

To the Editor: It is a sad day when *Connecticut Medicine* (1991; 55: 489-90) flaunts the straight *Pro-abortion choice* line through the pen of a guest editor, a lawyer from Planned Parenthood. It is a sad day when the AMA conspires in the killing of the unborn, and promotes this practice as an acceptable method of birth control.

The lawyer in question sees abortion as a part of "reproductive health care." Reproductive death? As doctors we all know when a new life begins, and we all know that abortion ends it. Enough of this editorial double-speak, please.

Daniel Gilmartin, M.D.

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Reassessment of External Insulin Infusion Pumps

ABSTRACT—Continuous subcutaneous insulin infusion (CSII) therapy using external infusion pumps provides an alternative to multiple daily injections (MDI) for insulin-dependent diabetics who require intensive insulin therapy. CSII allows for the delivery of regular insulin continuously at preset basal rates and at bolus doses, which can be varied in response to insulin needs of the patient. Intensive insulin therapy by CSII or MDI was administered to diabetics to improve control of their blood glucose levels and to assess its effects on the development of complications such as retinopathy and nephropathy. CSII appeared to be as effective as MDI in attaining near-normoglycemia and improving metabolic control in patients with insulin-dependent diabetes mellitus who required intensive insulin therapy. It was not clear, however, whether the improved control of the blood glucose levels resulted in the prevention or progression of the diabetic complications. The risks of having adverse effects, such as diabetic ketoacidosis or hypoglycemia, were higher with CSII as compared with MDI; both methods having higher risks of these complications in comparison to conventional insulin therapy. CSII may be beneficial for patients requiring intensive insulin therapy who may need greater lifestyle flexibility with regard to meal timing, work, and recreational scheduling.

S. STEVEN HOTTA, M.D., PH.D. AND DIANE ADAMS, M.D., M.P.H. DHHS, PHS, Agency for the Health Care Policy and Research (AHCPR), Center for Research Dissemination and Liaison, 18-12 Parklawn Building, Rockville, MD 20857, Tel.: 301/443-4100.

This report is available free of charge from the Information and Publications Division, Agency for Health Care Policy and Research, Room 18-12, 5600 Fishers Lane, Rockville, MD 20857.

The Month's Reading in Review

TIMOTHY B. NORBECK

- Reporting in *Reason Magazine*, James L. Payne notes that the propensity of congressional representatives to spend (as measured by the National Taxpayers Union) tends to rise the longer they are in office….The only exception is that first-timers tend to be slightly bigger spenders than second-timers….Referring to this issue, James C. Miller, III, Chairman of the Citizens for a Sound Economy, suggests that congressional term limits could reduce the rate of growth in federal spending by at least one-third.
- Last month this column described the term-limitation measure, Initiative 553, coming before Washington voters next month….Some critics of the measure suggest that it is a partisan effort headed by Republicans…."Not so", says Sherry Bockwinkel, executive director of Initiative 553 to limit terms for Washington's state and federal representatives….She says that "If you had to describe the group that created this, we were liberal Democrats"….According to the Wall Street Journal, the petition that put I-553 on the ballot garnered the fourth largest number of signatures in Washington's history….A survey by Moore Information shows that 70% of voters in Washington state favor term limits.
- The issue of assisting terminally ill patients to die will also be decided by voters this November in the state of Washington….On the ballot is an initiative which would allow a physician who is willing, upon request of a terminally ill patient, to help that patient die without unnecessary pain and suffering….In effect, passage of Initiative 119 would make Washington the first place in the world to legalize physician-assisted suicide.
- Nationally, a 1975 Gallup Poll found that 41% of respondents believed that a person with no hope of recovery and in great pain had a moral right to commit suicide….By 1990, that number had increased to 66%.
- Health care critics point to polls indicating that the American public believes that citizens receive better care outside of the United States in other industrialized countries….However, when asked in a recent 1991 AMA public opinion poll, "Do you think Americans receive better health care, the same health care or worse health care than people in other industrialized countries?": 51% reported better, 17% said it was the same, 19% claimed it was worse, and 13% were unsure.
- According to the Center for Human Resource Research, nearly half of all first-time mothers age 15-30 in the United States use alcohol and/or marijuana during pregnancy….Younger, less-educated women are more likely to smoke cigarettes or marijuana…. Older, better-educated women favor alcohol.
- Blue Cross and Blue Shield of West Virginia made history in October of 1990 by being the first Blues plan to go bankrupt….Those states today where total claims now exceed reserves include the Blues in New Hampshire, New Jersey, Rhode Island, Vermont and Western New York.
- From the book, *The Great Divide, How Females and Males Really Differ*: 81% of women and 67% of men visit a physician each year….39% of women and 20% of men survive until 85….52% of women and 48% of men visit a dentist each year….66% of female and 50% of male high school seniors think finding purpose and meaning in their life is extremely important to them.
- According to *Health Action Managers*, people who smoke have 18% higher medical claims than non-smokers and are 43% more likely to miss a week of work each year….Sedentary employees spend 30% more days in the hospital a year than active individuals and are 20% more likely to call in sick more than one week a year…. Seriously overweight workers are 48% more likely than their normal weight co-workers to have claims exceeding $5,000 in one year and are 29% more likely to miss more than a week of work a year.
- As reported in the *Wall Street Journal*, consultant Towers Perrin found that 12% of 135 large firms offer discounts, or impose surcharges, on employee insurance to encourage healthy habits such as exercise and discourage such behavior as smoking…But the consultant warns employers to avoid applying incentives to such things as high blood pressure or high cholesterol, which have "genetic components."
- Explaining to a reporter from *Sports Illustrated* why baseball player aren't overpaid Detroit Tigers outfielder Pete Incaviglia said: "People think that we make $3 million and $4 million a year….They don't realize that most of us make only $500,000."

From the Executive Director's Office

COUNCIL MINUTES

Wednesday, October 23, 1991

Attendance

Present in addition to the Chairman, Dr. Joseph C. Czarsty, were Drs. Ahamed, Beck, Blake, Blum, Bobruff, Brooks, Cottle, Deren, B. Fox, M. Fox, Franklin, Hosking, Kamens, Keating, McDonnell, Meridy, Orphanos, Parke, Petrie, Redmond, Sadowski, Sosa, Tesoro, Wetstone, Zanker, Zeppieri.

Also present were: Mr. Norbeck, Mrs. Lindquist, Ms. Ballou, Mr. Garofalo, Mrs. Connelly, Mr. Thompson (FCMA), Mrs. Norbeck (HCMA), Mr. Freberg (NHCMA).

Absent were: Drs. Dardick, Eslami, Freedman, Hollister, Lesnik, Parikh, Petro, Van Nostrand, Wolfson.

Introductions

Dr. Czarsty introduced two new councilors, Wayne F. Hosking, M.D., from Hartford County and Michael R. Tesoro, M.D. from Litchfield County.

Reports of Related Organizations

CPRO: Dr. Kamens reported that PRO office review is scheduled for initiation in January, 1992. At present time, however, no one knows what the regulations are going to be since they have not been written. HCFA has approved a pilot project, the Wisconsin Ambulatory Review Project (WARP) to look at certain elements of office review before it is initiated. Connecticut has been selected as one of six states to participate in the study. There are many things to be considered prior to starting the review, such as: what is available at the present time in physician's documentation in their office records? what are the appropriate things to be reviewed? and over what period of time should review be conducted in order to have scientific value? Also, it was to be understood that this review would be a study only. It is non-punitive. There would be no sanctions involved with this review and no disclosure of information about the physicians being reviewed to anyone, except to the individual physicians themselves who are volunteers in this program. They will be given information about themselves who are volunteers in this program. They will be given information about themselves as compared to a statewide average for each area reviewed. Four hundred physicians will be asked to volunteer approximately ten to fifteen of their charts so that they can be reviewed. It was VOTED to endorse, in principle, CPRO's involvement in WARP.

M.D. Health Plan: A communication from Jerome K. Freedman, M.D. reporting on a meeting of M.D. Health Plan was received as information. Guy Van Syckle, M.D., Medical Director of M.D. Health Plan, joined the Council to give an update on the activities of the Plan. He noted that the financial situation at the present time is very optimistic. He further stated that he will be leaving the position of Medical Director of M.D. Health Plan, since the position now calls for a full-time person and he is not interested in full-time employment.

The members of the Council expressed their gratitude to Dr. Van Syckle for the service he has rendered to his colleagues and to CSMS.

Report of the President

Disabled Workers Symposium: Dr. Redmond reported that he had attended the Fourth Annual Disabled Workers Symposium and stated that it was an excellent meeting and had an attendance of about 300 people and 30 exhibitors. He noted that Drs. Zeppieri and Deren and others responsible for arranging this symposium should be commended for this outstanding meeting.

CSMS Retreat: He reported that the planning committee, which consists of himself, Drs. Ahamed, Beck and Czarsty met and have set the date for the retreat for March 6, 7, 8, 1992 at the Saybrook Point Inn, Old Saybrook. The facilitator is Bruce Balfe from the AMA, and the participants would be limited to the following: three prior past presidents, Chairman of the Council, President, President-Elect, Vice-President, Secretary, Treasurer, Speaker and Vice-Speaker of the House of Delegates and one representative from each of the county medical associations. Tentative plans include a briefing meeting with the facilitator on Friday evening, and meetings on Saturday morning, Saturday afternoon and Sunday morning. Definitive scheduling and agenda items will be discussed at future meetings of the planning committee. A request for a budget of approximately $10,000 has been requested from the Fiscal Subcommittee for this retreat and will be acted on later on in the agenda.

Communication: He reported receiving a communication from Representative Naomi K. Cohen, Deputy Majority Leader of the State House of Representatives, concerning Public Act 91-105, "An Act Concerning Disciplinary Hearings Regarding the Safe Practice of Medicine" and commented on the Society's involvement in regard to this piece of legislation. It was VOTED to send Representative Cohen a letter outlining the Society's position in this regard.

Medicare: He stated that he attended a meeting of the Committee on Medicare which studied the User's Personal Identification Number (UPIN) Directory and it was determined that the directory was out of date and inaccurate.

Communication from New Haven County Medical Association: He reported that in response to a communication sent to all the county associations concerning combined CSMS and county membership and AMA membership for various categories of physicians, a letter was received from New Haven County Medical Association outlining their position on the various recommendations. As to the mandating AMA membership for all members of the Council and House of Delegates, the Board of Governors concluded that these motions would properly be acted upon in the House of Delegates when the amendments to the Bylaws are presented. As to joint county and state membership, it was concluded that mandating combined membership would be detrimental both to the county and state.

Health Care 2000

Dr. Wetstone reported on a new concept of health care being studied by the Hartford County Medical Association. He stated that the health care system is going to change and that we should have leadership and involvement in any proposal made. It is proposed to develop a consensus on the principles on which the future of health should be based. This project would entail HCMA staff preparing issue papers outlining the different models of health care systems that have been tried and then the steering committee will sponsor a series of public forums, possibly followed by a town meeting that will bring in key health leaders and a variety of models and permit interaction. As this process evolves, the people on this committee realize that it will have applications beyond the borders of Hartford County. The steering committee is composed of physicians, business leaders, health care providers, etc. As the program develops, additional information will be brought to the attention of the Council.

Report of the Executive Director

AMA Membership: Mr. Norbeck stated that he was happy to report that as of today, the official AMA membership count in Connecticut is 4,004 which means that we will not lose a delegate and commended the individuals involved in increasing AMA membership. He hoped that this number could be increased by another 100 members by year's end.

Disabled Workers Compensation Symposium: He reported that Drs. Redmond, Kamens spoke at the Symposium and he also had the opportunity to present medicine's side on health care costs.

Council on Aging: It was reported that Drs. Petrie, Wolfson and he participated in a panel discussion on health insurance at a meeting of the Council on Aging on September 26 and he commended Drs. Petrie and Wolfson on their presentations. Representatives of the Insurance Association of Connecticut (IAC) and CBIA were also in attendance at the meeting. He stressed the importance of physicians accepting speaking engagements and informing the public of medicine's point of view. He stated he has found audiences very receptive and pleased to receive information brought to them.

Dr. David Parke informed the Council that Mr. Norbeck represented CSMS at the Leadership Conference of the American Academy of Ophthalmology Meeting in Washington and spoke very eloquently about issues facing physicians in state legislatures throughout the country.

RBRVS: He further reported that it is expected that on November 10 or 11, HCFA will release the draft of rates under the RBRVS and it appears likely that the HCFA proposed decrease in the conversion factor will most probably end up at 3% as opposed to the 16% it sought.

Report of Committee on Legislation

Dr. Wetstone reported that on November 21, the committee would be having a meeting and issues arising from that meeting would be submitted to the next meeting of the Council. He reviewed the issues that would most likely be back during the 1992 Legislative Session on which positions had already been taken previously to ascertain that there was no change in attitude on these issues. Following are the items listed:

Allied health professionals expending their scope of practice—OPPOSE
Mandatory Aids Testing—OPPOSED
Mandatory Medicare or/and Medicaid Assignment—OPPOSED
Disclosures by physicians of any financial interests in health care facilities—SUPPORT
Triplicate prescriptions—OPPOSED
Bans an prescriptions—OPPOSE
Anti-smoking issues—SUPPORT
Increase in licensing fees—OPPOSE
Resident hours—MONITOR

It was VOTED to affirm the stated position of the Legislative Committee on the issues cited.

Statewide Physician Health Program Proposal

Edmund Hecklau, M.D., Chairman of the Committee on Physicians Health, joined the Council seeking endorsement for a proposal from the committee that CSMS establish a statewide physician health program (PHP) with a part-time paid director and a part-time paid coordinator, while at the same time preserving the existing county committee structure. Following lengthy discussion, it was VOTED that an Ad Hoc Committee be appointed to study the concept of a statewide physician health program and its cost effectiveness on the part of CSMS and report back to the Council.

Committee on Public Health

It was VOTED to approve the recommendation of the Committee on Public Health that CSMS adopt the following statement as a public position of CSMS for release to the press:

"In this time of economic retrenchment by the state government, the Connecticut State Medical Society supports the sound and compassionate priorities reflected in the actions of our State Commissioner of Health Services to retain crucial child and maternal health, vaccination, and vital records services, even at the cost of temporarily postponing routine licensure and renewal activities for most allied health professions."

NB.: *The foregoing is a summary of the proceeding and actions of the Council on October 23, 1991. Detailed minutes of the meetings are on file at 160 St. Ronan Street, New Haven, for the perusal by any interested members of the Society.*

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BOOK REVIEWS

The Development of Techniques and Treatments

By Martin Duke, M.D. 252 pp., illustrated. Madison, Conn., International University Press, 1991. $32.50.

Dr. Duke has written a small book for a very special audience. He has selected 29 common items from today's medical armamentarium, reviewed their history, and highlighted their development in a clear and easy-to-read style. The history of science and medicine can be an arcane discipline; this book demonstrated that it doesn't have to be.

This is not a textbook nor is it a reference book in medical history. It does not pretend to original historical scholarship; it is not designed to be studied as much as it is to be read and enjoyed. While the educated layman might enjoy reading it, it seems to be written primarily for the medical student and resident and the busy practitioner, especially the internist. The book will enhance the clinician's technical knowledge and expand his appreciation for all that has gone into what we take for granted in everyday practice. I suspect the author would also like to whet the reader's appetite for further ventures into the history of medicine.

The author has selected some of the clinicians' most common procedures and arranged them under three general topics—basic techniques, pharmacology, and basics of cardiology. The first section is devoted to the origins of vital signs, cardiopulmonary resuscitation, the electrocardiogram, and blood banking. The chapter on the recognition of fever as a symptom and the developement of the thermometer, the history of auscultation and the development of the blood pressure cuff, cover events that are not so well known but are well summarized here. The chapter on the development and evolution of the EKG from Einthoven's string galvanometer to the correlation with infarcts and arrhythmias is well done with the significant papers cited. On the other hand the chapter on transfusion seems incomplete. It illustrates some early attempts at transfusion but ignores some of the great discoveries, the foundation of modern blood banking, anticoagulation, sterility, and knowledge of the ABO - Rh antigens.

The second section of the book dealing with pharmacology and therapeutics is, in my estimation, less strong. The chapters on opium-morphine, iron, and atropine start with early descriptions but stop long before there is a connection made with modern pharmacology. The chapters on diuretics. pernicious anemia, and insulin are much more complete because they bring the reader to the roots of today's therapeutics. The chapters on leeches, music, and wine as "therapeutic modalities" seem to have been included as examples of "false starts" or "wrong turns" in the march of science. These topics are presented in terms of early expectations, but there is little analysis of their exclusion from mainstream medicine today.

The third and final section dealing with the foundations of modern cardiology is clearly the strongest. Much of the material has evolved within the lifetime of middle-aged physicians: I predict some readers will be saying "I remember..." as they read these chapters. The early stories tell of exercise as therapy, anticoagulation, the rauwolfias and early antihypertensives, and the development of quinidine and the antiarrhythmic medications, and finally the beta-adrenergic blockers. The closing chapters deal with aspects of cardiac surgery including pacemakers and heart valves; medical students and residents will find this section the most exciting because of its immediate relevance to their clinical rotations.

I must conclude by repeating a statement made earlier; the author has tailored this introductory book to a very specific audience—busy clinicians, particularly internists, medical students, and residents.

It was written to expand their knowledge of medical history, and help them understand what and who have gone on before them, and I suspect pique their interest to read further. Borrowing from the format of the *Readers Digest*, the author has abstracted and condensed years, sometimes hundreds of years, of experience tracing the history of some twenty of the most common tools, drugs, and technologies of modern medicine into a few readable pages.

Dwight F. Miller, M.D.
Director, Department of Laboratory Medicine
St. Mary's Hospital, Waterbury

CORRECTION

In the article "Diagnostic Nasal Endoscopy and Functional Endoscopic Sinus Surgery: An Update and Review of Complications" by Steven B. Levine, M.D., Alan J. Gill, M.D., Stephen R. Levinson, M.D., and Tom K. Coffey, M.D., published in the October issue, the following biography information was omitted.

STEVEN B. LEVINE, M.D., ALAN J. GILL, M.D.. STEPHEN R. LEVINSON, M.D. AND TOM K. COFFEY, M.D. practice Otolaryngology-Head & Neck Surgery in Fairfield and Trumbull, and are attending surgeons at Bridgeport Hospital and St. Vincent's Medical Center in Bridgeport.

IN MEMORIAM

BLANEY, CYRIL C., Boston University, 1940. Doctor Blaney was a general practitioner in Bridgeport for 38 years. Doctor Blaney was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Died September 14, 1991.

BUTLER, ROBERT W., Tufts Medical School, 1930. Doctor Butler was a medical director of Scovill Manufacturing Company from 1951 to 1972. He was a member of the New Haven County Medical Association, Connecticut State Medical Society and the American Medical Association. Died September 21, 1991.

CARVEY, EDWARD V., Yale University, 1935. Doctor Carvey was in private practice in Wethersfield from 1937 until his retirement in 1978. He was a member of the Hartford County Medical Association, Connecticut State Medical Society and the American Medical Association. Died October 17, 1991.

CREATURO, NICHOLAS E., Boston University, 1931. Doctor Creaturo was an internist in Bridgeport for over 50 years. He was a member of the Fairfield County Medical Association, Connecticut State Medical Society and the American Medical Association. Died October 3, 1991.

FIALKOFF, RUBEN, University of Havana, Cuba, 1948. Doctor Fialkoff was former chief of emergency services at Manchester Memorial Hospital. He was a member of the Hartford County Medical Association and the Connecticut State Medical Society. Died September 7, 1991.

HALL, WILLIAM E., Yale University, 1925. He was a practicing physician in Meriden from 1927 until his retirement in 1977. He was a member of the New Haven County Medical Association and the Connecticut State Medical Society. Died August 10, 1991.

KASSIM, SAMI E., Royal College Medicine, Iraq, 1947. Doctor Kassim was a pediatrician in Trumbull for over 35 years. He was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Died September 8, 1991.

LENKOWSKI, WILLIAM J., New York University, 1937. Doctor Lenkowski was a family practitioner in Waterbury for over 40 years. He was a member of the New Haven County Medical Association, Connecticut State Medical Society and the American Medical Association. Died October 12, 1991.

MILLER, HUGH K., College of Physicians and Surgeons, 1932. Doctor Miller was chief of obstetrics at Stamford Hospital from 1950 to 1966. He was a member of the Fairfield County Medical Association, Connecticut State Medical Society and the American Medical Association. Died October 12, 1991.

NAGOURNEY, DAVID, State University of New York, 1936. Doctor Nagourney was a family practitioner in Bridgeport form 1939 until retiring in 1988. He was a member of the Fairfield County Medical Association and the Connecticut State Medical Society. Died September 20, 1991.

PERLIN, LOUIS, University of Lausanne, 1959. Doctor Perlin practiced psychiatry in Meriden for 27 years. He was a member of the Middlesex County Medical Association, Connecticut State Medical Society and the American Medical Association. Died September 19, 1991.

TAYLOR, ROBERT N., Yale University, 1930. Doctor Taylor practiced ophthalmalogy and otorhinolaryngology from 1932 until retiring in 1975. He was a member of the New London County Medical Association, Connecticut State Medical Society and the American Medical Association. Died September 19, 1991.

CSMS PHYSICIAN PLACEMENT SERVICE

The Society maintains the Physician Placement Service as a *free* service to the medical profession, hospitals, and communities in Connecticut.

Opportunities **should be typed, double-spaced copy on letterhead and submitted to CSMS, Physician Placement Service, 160 St. Ronan St., New Haven, CT 06511 (203)-865-0587. These will be published as space permits and will be distributed to physicians making inquiries of such *opportunities.***

Physicians wishing to locate **in Connecticut may call the office requesting opportunities in their specialty. Also, candidates are invited to submit a resume to be kept on file with the Society. An announcement of a physician's availability will be published in two issues of *Connecticut Medicine* as space permits.**

Listing of physicians in the Placement Service does not in any way represent certification by the Society. Investigation of credentials and experience is the responsibility of those seeking applicants for positions.

Announcements on the Physician Placement Service page under Classified Advertising are charged at the regular Classified Advertising rate.

OPPORTUNITIES FOR PRACTICE

AMBULATORY CARE

Part-time physicians needed for Ambulatory care center in Hartford area. Family Practice, Internal Medicine, or Ambulatory care experienced preferred. Contact: Jeffrey Davies, M.D., (203) 688-8888.

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Connecticut Coastline wants Family Practice or Internal Medicine Physician now for full time outpatient medical facility. Full benefit package. Starting salary $95,000+. Contact Larry Frisa immediately, and provide CV, 21 Montauk Ave., New London, CT 06320. Phone (203) 447-2723.

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GASTROENTEROLOGY

Available July, 1992. Age 29. Nat'l Bds. AB Cer. M.D. Mount Sinai School of Medicine, NY. Int. & Res. at N. Shore Univ. Hosp. Memorial Sloan-Kettering Cancer Center, NY. Gastroenterology Fellowship at the Univ. of Miami Affiliated Hospitals. Prefer solo, group or assoc. practice in a large to medium size community. Write: Stephen David, M.D., 4101 Pinetree Dr., Apt 829, Miami Beach, FL 33140.

INTERNAL MEDICINE

Immediately available. Age 33. Licensed in CT. ECFMG and FLEX. AB elig. M.D., Universidad del Noreste, Tampico, Mexico; Int. and Res. Flushing Hospital, Flushing, Queens, NY, and Res. Maricopa County Hospital, Phoenix, AZ. Write William M. DiFederico, M.D. 13 Nott Lane, Essex, CT 06426

RADIOLOGY

Diagnostic Radiology. Available Fall 1991. Age 33. Licensed in CT, and NY. Nat'l bds. AB Cert. M.D. Univ. of Vermont, College of Medicine. Int. Waterbury Hosp. Health Center, Waterbury, CT. Res. Yale New Haven Hosp., New Haven, CT. Prefers group practice. Write: Jay Sokolow, M.D., 187 Willard St., New Haven, CT 06515.

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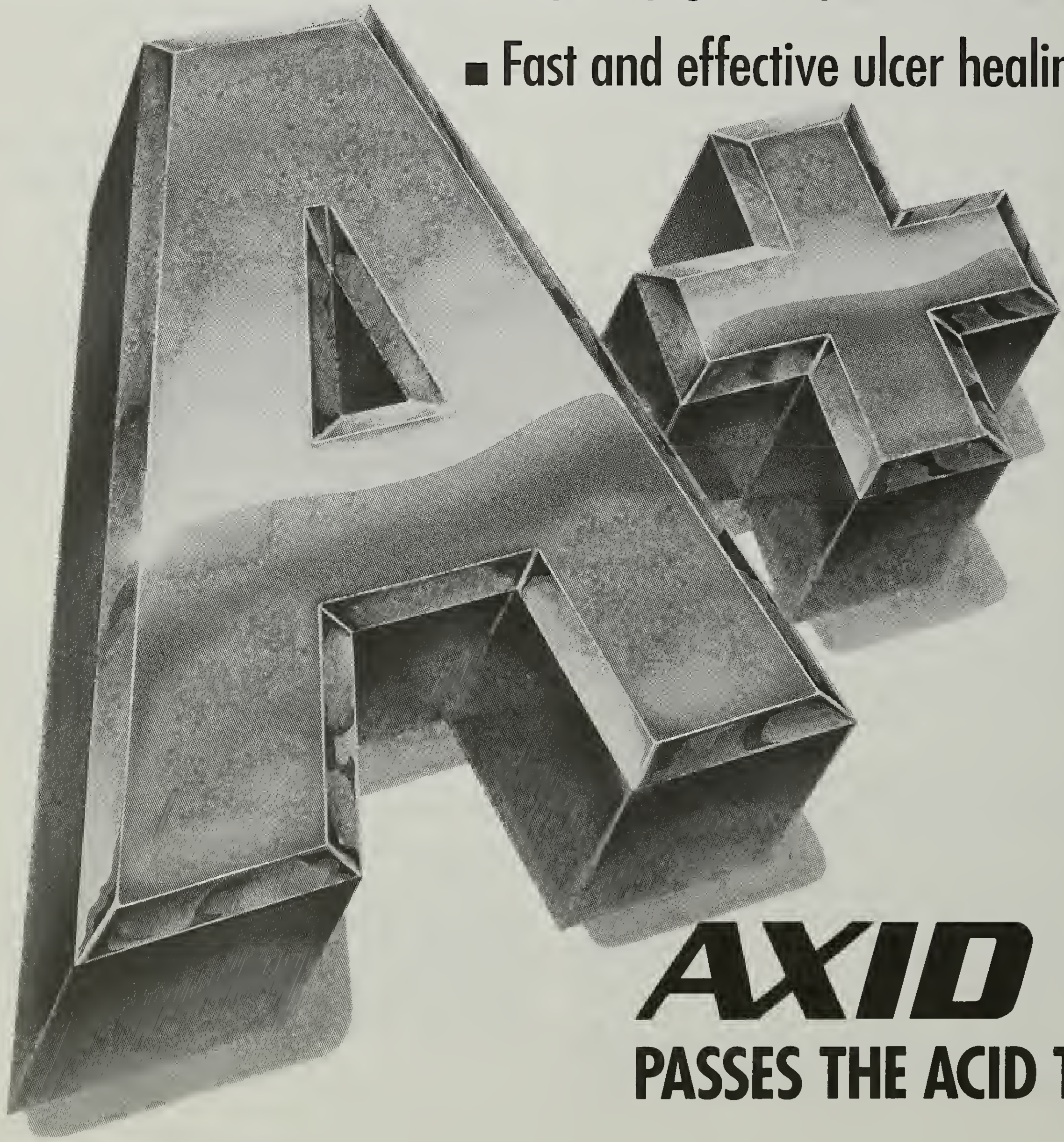

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Lifetime Psychiatric Illness and Premenstrual Syndromes

GRACE CHANG, M.D., M.P.H. AND KAREN A. HUTCHINSON-WILLIAMS, M.D.

ABSTRACT—The frequency of affective symptoms in most descriptions of premenstrual syndromes (PMS) suggests a potential etiologic link between menstrually-related mood changes and specific psychiatric disorders. The purpose of this study is to assess women presenting with "PMS" for lifetime psychiatric illness and PMS, according to rigorous diagnostic criteria comparable to those for "late luteal phase disorder," a proposed DSM-III-R diagnosis requiring further study. The women were interviewed with the Schedule for Affective Disorders and Schizophrenia Lifetime Version (SADS-L) and they kept prospective records of menstrual symptoms with the Moos Menstrual Distress Questionnaire - Form T (Moos MDQ-T). Of the 20 women evaluated, 85% had lifetime psychiatric illness and 30% had PMS. Careful psychiatric assessment is recommended in patients presenting with "PMS" as their chief complaint.

Introduction

SINCE its first medical description in 1931[1] the complexity of the premenstrual syndromes has been appreciated over nearly six decades of research. Lines of inquiry have included endocrinological, pharmacological, and psychiatric investigations. One point of convergence has been the possible relationship between premenstrual complaints and psychiatric illness.

This theorized relationship has been examined in two general ways. One line of inquiry has been to attempt to assess premenstrual problems in patients identified to have psychiatric problems. The second approach has been to assess psychiatric morbidity in women whose chief complaint is premenstrual syndrome. Most studies thus far have relied on retrospective reports of premenstrual symptom assessment, which is problematic because of attributional patterns of linking negative moods to the premenstruum,[2] social expectancy and demand characteristics,[3,4] biases in the processing of information about cyclicity,[5] or sterotypic beliefs about menstruation.[6] Moreover, only five studies have investigated the possible relationship between premenstrual symptoms and specific psychiatric disorders using explicit diagnostic criteria for both, but all (with the exception of a small subsample in one study) diagnosed premenstrual mood changes with retrospective methods, which have been shown to be invalid.[7] It is still unclear whether a reciprocal relationship between psychiatric illness and premenstrual problems exists.

"Late luteal phase dysphoric disorder" is designated as a proposed diagnostic category requiring further study in DSM-III-R. The essential feature of this disorder is a pattern of clinically significant emotional and behavioral symptoms that occur during the last week of the luteal phase and remit within a few days after the onset of the follicular phase. Diagnostic criteria require that the disturbance seriously interferes with work or usual social activities, that the disturbance is not an exacerbation of the symptoms of another disorder, and that symptoms are confined by prospective daily ratings.[8] The purpose of this pilot study is to clarify the reported association between psychiatric illness and premenstrual syndromes[9,10,11] using a prospective measure of premenstrual symptoms, the Moos Menstrual Distress Questionnaire - Form T (Moos MDQ-T), and a highly reliable structured diagnostic interview for lifetime psychiatric illness, the Schedule for Affective Disorders and Schizophrenia - Lifetime Version (SADS-L).[12,13,14] We predicted that prospective assessment of premenstrual syndromes would result in fewer diagnoses of PMS and that psychiatric assessment might reveal previously undiagnosed morbidity.

GRACE CHANG, M.D., M.P.H., was Assistant Professor at the Yale University School of Medicine when this work was completed. She is currently with the Department of Psychiatry, Harvard Medical School and the Brigham and Women's Hospital. KAREN A. HUTCHINSON-WILLIAMS, M.D., is Assistant Professor of Obstetrics and Gynecology and Medicine (Endocrinology), Yale University School of Medicine.

This work has been presented in part at the 45th Annual Meeting of the American Fertility Society, San Francisco, California, November 1989. It has been supported in part by the Veterans Administration and Robert Wood Johnson Clinical Scholars Program. It does not represent the opinion or policy of either the Veterans Administration or the Robert Wood Johnson Foundation.

Address reprint requests to Dr. Chang at 75 Francis Street, Boston, MA 02115

Materials and Methods

Twenty-five of the women evaluated at the Yale University School of Medicine PMS Clinic in the Division of Reproductive Endocrinology between September 1987 and December 1988 agreed to participate in a study investigating the relationship between PMS and psychiatric illness. Over 75% of the study population was self-referred, presenting with the chief complaint "PMS," and all subjects gave informed consent. Each volunteer completed an extensive health history and was interviewed thoroughly by one of us (KHW) to exclude concomitant medical problems, such as endocrinopathies. Medical records were reviewed. None of the women had any significant health issues, precluding their participation. None received any financial inducements to participate.

The demands of the study were rigorous. Each volunteer was required to keep prospective symptom records, the Moos MDQ-T for at least two consecutive menstrual cycles. The Moos MDQ-T is a 47-item self-report questionnaire of menstrual symptoms. These records were reviewed monthly with the patient. Measurement of daily basal body temperature was also required. This was necessary in order to define more precisely the follicular (preovulatory) and luteal (postovulatory) phases of the menstrual cycle because there was variability in cycle length among different subjects. A 48-hour period around the peak mid-cycle temperature elevation was designated the "periovulatory window." Data were not considered from this period. Days seven to 10 of the menstrual cycle were chosen to represent the late follicular phase (designated intermenstrual or I). The late luteal phase (designated premenstrual or P) was represented by data collected four to six days before the onset of menstruation. The diagnosis of PMS was made employing guidelines established by the National Institute of Mental Health: a marked change in intensity (at least 30%) of symptoms measured from cycle days five to 10 compared to the six-day interval prior to menses for at least two consecutive cycles.[15] A Moos MDQ-T score of <70 was considered to represent an asymptomatic period.[16] Therefore the diagnosis of PMS was applied to any patient if her premenstrual MDQ-T score exceeded an intermenstrual score of <70 by 30%.

Subjects were given the SADS-L by a psychiatrist (GC) who was unaware of their PMS status at the time of psychiatric interview and rating. The SADS-L, a highly reliable structured diagnostic interview for lifetime psychiatric illness, was administered randomly throughout the menstrual cycle. The diagnoses generated by this instrument are stable and not vulnerable to the fluctuations of premenstrual complaints.[12,13,14]

Results

Twenty-five women completed the SADS-L interview and 20 provided at least one month's daily diaries. Of the 20 who cooperated with the PMS evaluation, 17 completed Moos MDQ-T diaries for at least two cycles. Results will be reported for the 20 subjects who participated in all phases of the evaluation.

The subject's demographic characteristics are summarized in Table 1.

Figure 1 depicts the MDQ-T scores of one of the

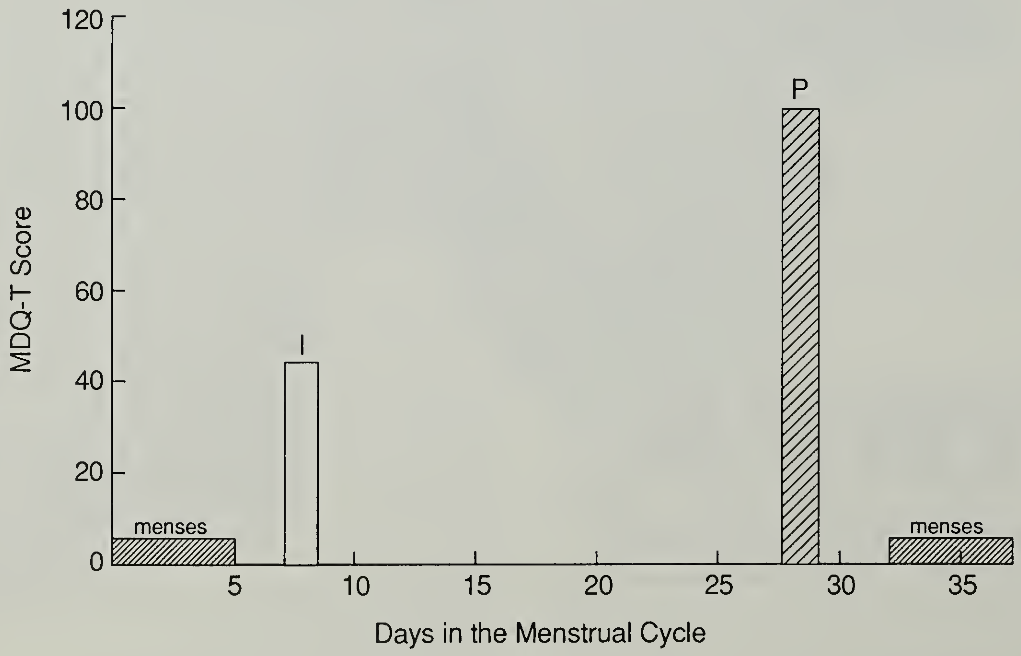

Figure 1.
Intermenstrual (I) and Premenstrual (P) scores in a women with PMS. Note that the P score is greater than 30% higher than the I score which is less than 70 (see text for details).

Table 1

Subject, Demographic Characteristics (n=20)

Race	Caucasian	95%
	African American	5%
Mean age	35.8 years (range 26 to 44)	
Marital status	Married	70%
	Divorced	20%
	Single	10%
Children		65%
Childless		35%
Employment status	Employed	85%
	Unemployed	15%
Education	HS graduate	30%
	Attended college/trade school	30%
	College graduate	15%
	Graduate/professional degree	25%

women with rigorously defined PMS. Of the 20 subjects, six (30%) satisfied NIMH diagnostic criteria for PMS, as well as diagnostic criteria for the proposed Late Luteal Phase Dysphoric Disorder.

An 85% rate of positive lifetime history of psychiatric illness was noted in the study group. Diagnoses among the 17 women with psychiatric illness clustered around major or minor depressive disorders (47%) or anxiety disorders (35%). Whereas 30% of the subjects satisfied diagnostic criteria for PMS, 85% satisfied criteria for at least one Research Diagnostic Criteria (RDC) psychiatric diagnosis. Four (20%) women had both PMS and at least one RDC psychiatric diagnosis. Figure 2 summarizes the relationship between PMS and psychiatric diagnoses in the study population.

Of the 14 women diagnosed to have either major or minor depression, two were currently ill at the time of interview. Half of the remaining 12 women with histories of depression had depressive symptoms between two and 16 weeks prior to their psychiatric evaluation. Of the eight women who satisfied RDC for the anxiety disorders, including generalized anxiety and panic disorders, four were currently ill. Four women were found to have had nonconcurrent diagnoses of both major or minor depression and panic or anxiety disorders by history.

The psychiatric status of the women who satisfied both PMS and RDC psychiatric diagnostic criteria showed a preponderance of active psychiatric illness. Three had current psychiatric disorders at the time of PMS evaluation, two with panic disorder and one with minor depression. Two of the three were receiving psychotropic medications including an anxiolytic and antidepressant.

Discussion

The 85% occurrence of lifetime psychiatric illness in 20 women whose chief complaint was premenstrual syndrome is noteworthy. Moreover, only 30% of our sample, all of whom complained of "PMS," satisfied diagnostic criteria for this entity. Among the 17 women with lifetime psychiatric illness, six were currently symptomatic with anxiety or depressive disorders, and six had depression within four months of their psychiatric and PMS evaluation. Ten (50%) subjects were involved in psychotherapy at the time of entry into our study.

Extrapolation of our findings must be limited. The small sample size of the study and the possible assembly bias limit generalization to all premenstrual syndromes. As most were self-referred for treatment and all agreed

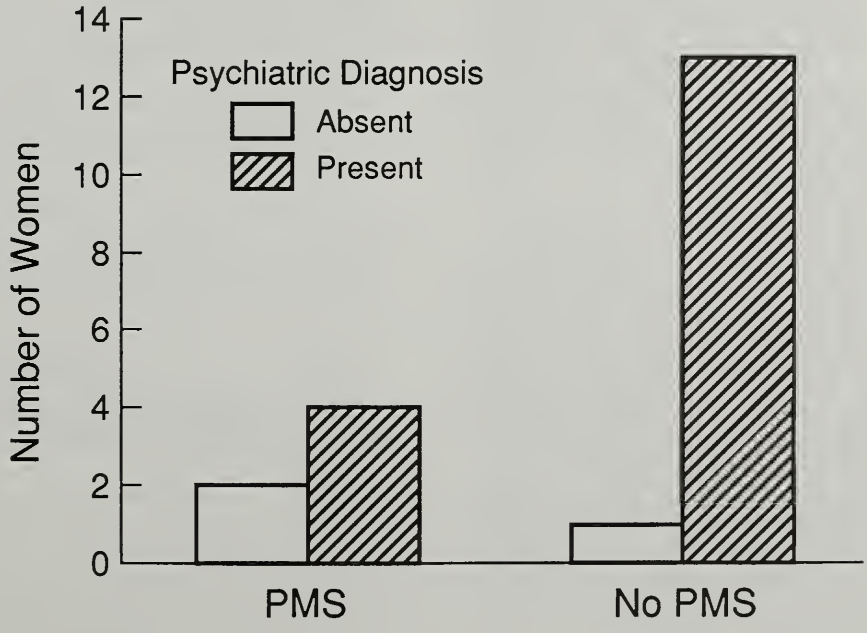

Figure 2.
The presence of psychiatric illness is demonstrated in relation to the presence (left) or absence (right) of PMS.

subsequently to complete the extensive study evaluation, the subjects probably represent a self-selected, highly motivated group of women without endocrinopathy. Future investigation should include PMS and psychiatric assessment with endocrine data in both a larger sample of women presenting with "PMS" and a control group without that complaint. However, the women under discussion may be typical of patients who do present to subspecialty clinics. The demographic composition of this sample is comparable to that of other subspecialty PMS clinics.[17]

During the course of investigation, another possible limiting factor came to light. The degree of involvement necessary for completion of daily diaries may have deterred subjects who themselves had doubts about their PMS status. In all, 25 women cooperated with the psychiatric assessment, but only 20 (80%) finished the prospective premenstrual symptom diaries for the prescribed period of time. All five women who completed only the SADS-L actually had lifetime histories of depression and one was currently depressed. They may have chosen not to finish the PMS evaluation because of their own insight into the functional nature of their difficulties. Our observations are supported by the findings of other investigators who have noted increased psychiatric morbidity in subjects who complain about PMS.[18] Fortunately, we have information about the PMS status of our subjects, only 30% of whom satisfied diagnostic criteria using prospective diaries.

While there may be a relationship between recent or remote psychiatric illness, particularly affective and anxiety disorders, and the perception of premenstrual syndrome, we do not find a reciprocal relationship between prospectively diagnosed PMS and lifetime psychiatric illness. This is in agreement with early studies of psychiatric inpatients and outpatients where investigators failed to demonstrate a convincing relationship between psychiatric disease and PMS.[19,20,21,22,23] Indeed, Endicott has suggested that premenstrual changes characterized by a depressive syndrome may, in fact, represent a mild or subclinical manifestation of an affective disorder.[9,10]

The data from our study support the hypothesis that premenstrual syndromes and psychiatric illness may be concurrent but separate disorders. Careful assessment of psychiatric morbidity is recommended in all women whose chief complaint is "PMS," since the etiologic basis of the complaint may lie in the realm of menstrual exacerbation or entrainment of psychiatric symptoms. In addition, the diagnosis of PMS requires scrupulous prospective evaluation of symptoms according to standard criteria, such as those listed for the proposed diagnosis, Late Luteal Phase Dysphoric Disorder. Acquiring prospective information from patients, who may be less motivated than study volunteers, may be problematic. Nonetheless, accurate diagnosis is essential in understanding and treating the premenstrual syndromes, an enigmatic disorder which has thus far defied clarification from a pathophysiological standpoint.

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Replacing an Old Drug with a New One

ROBERT P. FERGUSON, M.D.

ABSTRACT—One of the constants facing the individual who practices clinical medicine is the evaluation of the continuing flow of new pharmaceutical products. It is a formidable challenge to use the most up-to-date therapeutic agents judiciously and with proper monitoring.

This commentary will discuss issues for the practitioner to consider when faced with the prospect of replacing an old drug with a new one. It will attempt to develop a framework to facilitate rational decision-making in this context.

Introduction

AT a recent University of Connecticut Primary Care Internal Medicine Residency pharmacology seminar, residents were presented with the following case:

> The lay press has been buzzing with reports about a new drug that has taken Europe by storm. Gonadoinositol tolfenamic acid (GOINTO), a third generation tranquilizer/mood elevator, has been found to be effective and safe in a clinical trial conducted in a group of middle-aged Norwegian executives. Recently, a US pharmaceutical firm with a reputation for agressive promotion, has obtained a license to market the long-acting version of this drug in the United States under the brand name, GOINTO LA.
>
> The pharmaceutical firm's representative calls on you in your office and details this drug, urging you to try it on your chronically depressed, elderly nursing home patients.
>
> Your response should be:
>
> A. "I'll take a gross of samples, three dozen pens and a bumper sticker, GET MELLOW WITH GOINTO LA."
>
> B. "Is there, by chance, a company sponsored symposium in Aruba?"
>
> C. "I need to thoroughly review the scientific data."
>
> D. "I'm from New England, call me back in two years."

Although some residents said they were tempted by choice A, most chose C. The faculty's choices were evenly divided between B & C. The conservative program director chose D, but added that he would wait five years if the drug had been approved during a Republican administration.

This fictitious scenario was not that far removed from a common dilemma facing physicians: a pharmaceutical product becomes available for general distribution in the United States with favorable reports of safety and effectiveness. However, its advantages over current therapy are not clear.

The ability independently and critically to evaluate new pharmaceutical products is a necessary skill for good medical practice. In time, a practitioner is likely to be using mostly new drugs developed after he or she has completed formal medical training. This commentary will review and discuss issues to consider when comparing the safety and effectiveness of a new pharmaceutical product to an older version.

Effectiveness

Various reasons why a new drug may be more effective than existing alternatives are outlined in Table I. A drug may have greater efficacy in achieving a desired therapeutic effect. The most recent generation of lipid-lowering agents are good examples. However, such a straightforward difference is the exception, not the rule. Drugs with improved delivery systems may show significantly favorable pharmacokinetics, causing smoother and sustained pharmacodynamic effect. Studies of once-a-day nifedipine gastrointestinal therapeutic system formulation have demonstrated more consistent plasma concentrations and consequent therapeutic responses.[1,2] However, the evidence of improved effectiveness of a new controlled-release preparation in comparison to an earlier multidose product frequently is lacking at the time

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Table 1

Reasons Why a New Drug May Be More Effective

- Improved efficacy
- Improved consistency of blood levels

- Improved compliance
- Improved convenience

- Treatment of new disease
- New treatment of an old disease
- Treatment of more than one disease

- Placebo effect

of the new drug's marketing. This explains why controlled-release drug promotions frequently blur improved efficacy with related but separate issues of improved compliance and convenience.

A number of studies have demonstrated excellent compliance with once-a-day drug dosing.[3,4] However, the physician should be cautious when applying such reports to individual patients since the study model may not reflect practice realities. The study by Eisen et al, for example, did not charge patients for their medications,[3] an important point since multidose regimens often are significantly less expensive than controlled-release preparations. New drugs with once- or twice-a-day dosing schedules are more convenient than more frequent dosing alternatives. Presumably, most patients would prefer to take a drug less often. Since infrequent dosing is often a trade-off for increased cost, the patient should be informed of the cost of this convenience.

Although small in number in comparison, some new drugs are highly likely to demonstrate increased effectiveness because of few existing therapeutic alternatives, eg, as in the treatment of AIDS. Drugs may also be more effective if they offer a new approach to an old disease. Deprenyl is a selective monoamine oxidase inhibitor that lacks pressor effects at low dosage. Since monoamine oxidase activity and subsequent free oxygen radical formation are felt to play a role in the pathogenetic nigral degeneration of Parkinson's disease, the use of deprenyl was studied to see if it could prevent Parkinson's disease progression. A report by the Parkinson study group confirmed the great promise of this approach.[5] The fact that this drug has been utilized suboptimally is a testimony to the effect of unrealistic physician expectations when using a new drug (and, perhaps, to ineffective promotion).[6]

Drugs can be more effective when used to treat conditions in addition to the primary one targeted, ie, treatment of comorbidity. Calcium antagonists are excellent agents for the concomitant treatment of hypertension and atherosclerotic heart disease. Converting enzyme inhibitors are effective antihypertensive agents and also may favorably effect the course of diabetic nephropathy, thus appearing to be well suited for the treatment of the diabetic hypertensive.

Finally, increased effectiveness may be result from the substantial placebo effect inherent in using new pharmaceutical products. Avorn noted the importance of this effect on the prescribing habits of physicians.[7] My experience with residents in training has been similar and may explain their propensity toward using the newest and latest drugs in their clinic practices. Physicians realize early that newness alone is important, reaffirming the principle that doctors should use a new drug while it still works!

Safety

Reduced side effects are the most frequently invoked factor in rationalizing the development of new pharmaceutical products. Thus, the ability of the physician objectively to evaluate promotional claims regarding safety is essential. Table 2 outlines reasons why a new drug may be safer than an old one. The central nervous system depressant effects of reserpine at higher doses limited its therapeutic usefulness and led to the development of other central-acting antihypertensive agents which had fewer adverse effects on cognitive function. Better drug delivery systems can lead to more sustained levels and reduced side effects caused by fluctuations in drug effect. This would seem especially important when side effects are dose dependent. New drugs may also be better tolerated than existing alternatives because of differences in elimination or because of improved selectivity of pharmacologic effects.

The absence of adverse biochemical effects in a new drug that were present in an older version is a frequent promotional claim. The short-term use of thiazides has been shown to lead to serum elevations in low-density lipoproteins and cholesterol. Advertising for indapamide has focused on its more favorable metabolic side effect

Table 2

Reasons to Expect Improved Safety in a New Drug

- Evidence in testing that the new drug causes less dose-related side effects.
- Expected improvement in drug elimination.
- Improved selectivity of pharmacologic effect.
- Absence of idiosyncratic biochemical effect during testing of the new drug that was present in the old.

Table 3

Safety Concerns Inherent in New Products (Hidden Dangers)

- Low frequency adverse effects.
- Population differences not previously identified.
- Uncertainties over dosage.
- Change in indications.

profile than that of the thiazides. A similar approach has been taken in enalapril promotions. However, the significance of thiazide-related lipid effects has been challenged.[8,9] It is important for the physician to be aware of the promotional context in which many of these safety comparisons are made. At times, the vigor of a pharmaceutical company's attempts to discredit the opposition exceeds acceptable bounds. Recently, the manufacturers of lisinopril published a correction about their claim that lisinopril had fewer incidents of rash and taste disturbances than captopril.

Conversely, when considering new drug safety, the physician should be aware of the dangers inherent in using products with less than established track records. This phenomenon was described by Barr in 1955.[10] He pointed out that the onslaught of new pharmaceutical preparations that had flooded the American market after World War II often left the physician unprepared to deal safely with these new products because of "hidden danger." This issue remains important today. In 1988, a European study reviewing 3,521 adverse drug reactions in nonsalicylate, nonsteroidal, anti-inflammatory drugs over a 16-year period, found that the drugs that had been on the market longest had the lowest risk of adverse reactions, even controlling for under-reporting of adverse events in older drugs.[11]

The increased frequency of adverse drug reactions that may be reported during early usage of drugs is related to a number of factors (Table 3). Premarketing requirements usually include testing of a drug for safety in only a few thousand patients. Thus, an adverse reaction destined to occur in one in 10,000 patients is not likely to be recognized either in testing or when early general utilization is limited. As distribution widens and utilization increases, spontaneous reporting of previous unknown adverse drug reactions may occur. Arguably, the more successful a drug is, the more low-frequency adverse drug reactions are likely to be observed. Zomepirac was introduced in November 1980 as a nonsteroidal anti-inflammatory agent marketed as an analgesic. Prior to release, it had been tested in 3,600 individuals with an acceptable safety record, confirmed by objective sources.[12] However, within six months of release, the first case of anaphylaxis was reported.[13] Over the next two years, there were over 200 reports of anaphylactic reactions with at least five fatalities.[14] The drug was voluntarily removed from the market by the manufacturer in March 1983, slightly more than two years after its release.

Increased adverse reaction reports with new drugs can also be explained by consumer population differences. During testing, study populations may not have been representative. The presence of high levels of comorbidity in the elderly, as well as the physiologic changes of aging, may cause intolerance to a drug that was well tolerated in robust middle-aged test subjects. Benoxaphren was released in the United States after testing and marketing in Europe and South America. However, the enthusiasm for its use diminished after reports in Europe of fatal cases of hepatotoxicity, primarily among the elderly.[15] It was removed from the market voluntarily by the manufacturer after two years of use in the United States (perhaps choice D was the correct seminar answer).

At the time of the release of a new drug on the US market, the pharmaceutical manufacturer must demonstrate the efficacy of its product. This may help to explain why the recommended initial doses of drugs may sometimes prove excessive. Fluoxetine was released in1988; it has recently been advertised as the antidepressant most frequently prescribed by psychiatrists in the United

Table 4

Reasons to use a new drug

- You have one of the drug company's pens
- The detail man took you to dinner
- Your patient asked for it after reading about it in a grocery store check-out line
- You attended a company sponsored and organized symposium
- The advertisement caught your eye
- You like to try new things

Good reasons to use a new drug

- There is a more convenient dosing schedule than previous versions
- It was favorably discussed at a company sponsored but not organized symposium
- It received a good evaluation in a nonpeer review journal

Better reasons to use a new drug

- Good studies in peer review journals showed improved safety or efficacy in certain clinical situations
- Objective sources recommended the drug
- Independent symposia gave a favorable review
- There is good reason to believe that your patient will have better compliance with this medication
- It is less expensive than the alternatives.

States. The success of this product is in part due to its apparent low side effect profile compared to other available antidepressants. Initial prescribing recommendations included a starting dose of 20 mg a day, which could be increased to a maximum of 80 mg a day. In 1990 increasing reports of toxicity led the *Medical Letter* consultants to recommend that the starting dose be reduced to as little as 5 mg a day because of adverse effects.[16]

Adverse reactions may also increase when a drug is used for unapproved indications. Physicians may use a new drug for unapproved conditions because medical practice may change more rapidly than the FDA approval process. Lack of familiarity by the manufacturer and the practitioner with use in different settings for different indications may lead to further risks not previously identified.

Costs

The apparent advantage of a new drug over an old drug has to be weighed against the increased cost likely to be reflected in the price of the new product. The difference may be significant particularly when the older drug is available in a generic form. Because of research and development, as well as promotional costs, new drugs are usually more expensive. When the advantages of a new drug are marginal or of questionable clinical significance, the relative importance of cost in making decisions increases. Cost differences can be stunning. According to Thompson, the annual wholesale cost differences of antihypertensive medications at recommended starting doses may vary between $504 and $1.42![17]

A new drug that is expensive is more likely to have an adverse effect on the success of the treatment if the increased cost decreases compliance. The few studies relating compliance and cost have suggested that cost is a major factor in compliance and that, in certain situations, cost is more likely to affect compliance than dosage frequency.[18,19]

Conclusion

Practicing state-of-the-art internal medicine requires familiarity in the use of new products released by the pharmaceutical industry. Acting as the patient's advocate, the physician must objectively compare new products with old products and understand the advantages and risks of trying something new. There are many reasons to replace an old drug with a new drug. In Table 4 I have cited and ranked a number of the explanations I have heard from medical residents over the last 10 years about why they are using a new drug. Whatever the reasons physicians must realize that they are participating in a process where monitoring and staying abreast of current information is crucial for proper medical care.

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Antibiotic Prophylaxis of Lyme Disease Following Recognized Tick Bite

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ONE of the most frequently asked questions concerning the prevention of Lyme disease is what to do about persons in endemic areas who have had a recognized tick bit. Although the prophylactic use of antibiotics for a tick bite may be a common, albeit controversial, medical practice in some areas,$^{1-3}$ a definitive risk- or cost-benefit analysis of the practice does not exist. The recent NIH workshop on the "state of the art" of diagnosis and therapy of Lyme disease held in Washington, DC, 25-26 March 1991, stated that "The use of antibiotics, as with all medicines, is associated with some risk of adverse reactions and untoward side effects. Thus, prophylactic use of antibiotics could be very costly in terms of potential side effects as compared to case prevention. At this time, antibiotic prophylaxis for prevention of Lyme disease among the general population is not indicated.... At the present time it does not appear necessary to prescribe antibiotics solely on the basis of a tick bite, although this is being investigated." In conclusion, it was stated that "The decision as to whether prophylactic treatment of a patient with a tick bite is warranted is ultimately up to the attending physician and should be made on a case by case basis."[4] To help health care workers and others make rational decisions on prophylaxis, we provide a summary of the available epidemiologic evidence on this subject, including the results of five clinical trials and two observational studies, some of which are unpublished or have been published in abstract form only:

Agre F, Schwartz RM: The value of early treatment for the prevention of Lyme disease. *Am J Dis Child* 1991; 145:391 [Abstract 175].

Clinical Trial: These researchers reported the results of a randomized placebo-controlled double-blinded prospective study of patients between three and 19 years of age presenting with *Ixodes dammini* tick bites over a three-year period in New York. Subjects were randomized to receive oral antibiotics (penicillin or tetracycline) for 10 days or placebo and were followed for 2.5 years for development of clinical evidence of Lyme disease. Tests for antibodies to *Borrelia burgdorferi* (IFA) were performed on paired serum specimens taken at times zero and six weeks. Ticks were not examined for infection rates with *B. burgdorferi*. Of the 89 patients in the treatment group, none developed clinical evidence of Lyme disease and none seroconverted. Four (4.4%) of the 90 patients in the placebo group had a "weakly positive" rise in antibody titer, and one of these (1.1%) developed erythema migrans. Of the remaining three patients with titer rises, one had a nonspecific ("flu-like") illness and two had no symptoms. In the 2.5 year follow-up period, no patient developed later stage Lyme disease. NOTE: The authors recently provided CDC with the following additional information. The study area was northern Westchester County. The four seroconversions by IFA were conversions from <1:8 to 1:32.

Costello CM, Steere AC, Pinkerton RE, Feder HM Jr: A prospective study of tick bites in an endemic area for Lyme disease. *J Infect Dis* 1989; 159:136-9.

Clinical Trial: These researchers reported the results of a randomized placebo-controlled double-blinded prospective study of patients presenting with *I. dammini* tick bites in Connecticut during 1986. The treatment group received oral penicillin for 10 days. Tests for antibodies to *B. burgdorferi* (EIA) were performed serially for six months. Ticks were examined for spirochetes using fluorescence microscopy. Patients who developed illness during the study were examined by their physician. Six to 12 months following their *I. dammini* bite, patients were questioned by

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Reprinted with permission from the *Bacterial Zoonoses Branch, Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, Center for Disease Control*, Vol. 2, No. 6, August 1991.

mail regarding symptoms of illness. Of 68 patients initially enrolled in the study, 56 (82%) completed the study protocol. No seroconversions were observed. None of the 27 patients in the treatment group developed Lyme disease. One treated subject developed an allergic dermatitis after five days of penicillin, but subsequently completed the 10-day treatment. One (3.4%) of the 29 patients in the placebo group developed erythema migrans and constitutional symptoms 14 days following the tick bite (this tick was not suitable for study, so it was not known whether it was infected). The patient responded completely to 10 days of oral doxyclycline and had no recurrence of the illness. She remained seronegative. Twenty-one of the 48 *I. dammini* found on patients could be tested for infection (the rest were too desiccated for study), and six (29%) of these were positive for spirochetes compatible with *B. burgdorferi*. These six infected ticks included three each from patients in the treatment and placebo groups. None of these six patients developed Lyme disease. None of the 12 patients who dropped out of the study developed symptoms of Lyme disease.

Falco RC, Fish D: Ticks parasitizing humans in a Lyme disease endemic area of southern New York State. *Am J Epidemiol* 1988; 128:1146-52.

Observational Study (Retrospective): These researchers identified 126 ticks submitted by bite victims in Westchester County, New York, during 1985. Ninety-six (76.2%)of these were identified as *I. dammini*, either larvae, nymphs, or adults; the remainder were *Dermacentor variabilis* or *Amblyomma americanum*. Infection rates of ticks with *B. burgdorferi* were not determined. Bite victims were contacted for follow-up information 7-22 months after the tick bite. Retrospectively, 31 (44%) of 71 *I. dammini* bite victims from whom information was obtained had received prophylactic antibiotics following their bite. None of these 31 persons reported illness following their tick bite. Of the 40 *I. dammini* bite victims from whom information was obtained and who had not received prophylactic antibiotics, two (5%) had been diagnosed with Lyme disease. Both of these reported having been diagnosed with erythema migrans at the site of the tick attachment, from several days to two weeks following removal of nymphal *I. dammini*. No illnesses were attributed to *Dermacentor* or *Amblyomma* bites.

Gerber MA, Shapiro ED, Persing DH, Feder HM, Luger SW: Risk of developing Lyme disease after a deer tick bite. IV International Conference on Lyme Borreliosis. Stockholm. Book "A," 1990, p. 175 [Abstract M/TU-P-131].

Observational Study (Prospective): These researchers reported the results of a study of victims of *I. dammini* bites in southeastern Connecticut. Subjects were questioned serially for the presence of signs or symptoms of Lyme disease for three months following their tick bite. Tests for antibodies to *B. burgdorferi* (EIA) were performed serially for three months. None of the 39 enrolled subjects received antibiotic therapy during the three month evaluation period and none developed Lyme disease or seroconverted. Ticks were tested for evidence of infection with *B. burgdorferi* using PCR. Eight (32%) of 25 ticks examined were infected with *B. burgdorferi*. NOTE: This was a preliminary study to Shapiro *et al.* (1991), described below.

Nadelman R, Forseter G, Horowitz H, Fish D, Welch P, Marcus R, Bittker, Pavia C, Wormser G: Single dose doxycycline as prophylaxis for Lyme borreliosis after *Ixodes dammini* bites in a Lyme endemic area. IV International Conference on Lyme Borreliosis. Stockholm. Book "B," 1990, p. 34 [Abstract TH-L-12].

Clinical Trial: These researchers reported the results of a randomized placebo-controlled double-blinded prospective study of patients presenting with *I. dammini* tick bites in Westchester County, New York. Subjects were randomized to receive a single dose of either 200 mg doxycycline or placebo. Tests for antibodies to *B. burgdorferi* (IFA), blood cultures for *B. burgdorferi*, and evaluations for clinical evidence of Lyme disease were performed serially for six weeks. A total of 161 subjects had been enrolled at the time of this publication but the results had not been decoded. Of these, 132 were evaluable. Of these 132 subjects, 72 (55%) removed nymphal *I. dammini* and 60 (45%) removed adult *I. dammini*. Fifty-seven (43%) of these 132 subjects removed engorged *I. dammini* (35 nymphs, 22 adults). Two (1.5%) of the 132 evaluable patients developed erythema migrans. A third subject had an "influenza-like" illness with atypical rash and seroconversion. Thus a total of 3 (2.3%) of 132 evaluable patients developed clinical evidence of Lyme disease. Another 16 (12%) of these 132 subjects developed "influenza-like" illness without seroconversion. No asymptomatic subjects seroconverted. One unevaluable subject (due to multiple tick bits) developed a nonspecific ("influenza-like") illness with a positive blood culture for *B. burgdorferi*. Ten percent of subjects experienced possible adverse drug effects, including nausea, vomiting, or diarrhea. NOTE: The authors recently provided CDC with the following additional information: this study is ongoing and the results have not been decoded.

Shapiro ED, Gerber MA, Persing DH, Luger SW, Feder HM: Risk of developing Lyme disease after a deer tick bite in an endemic area. *Pediatr Res* 1991; 29:185A [Abstract 1091].

Clinical Trial: These researchers reported the results of a randomized placebo-controlled double-blinded prospective study of patients presenting with *I. dammini* tick bites in southeastern Connecticut during 1989 and 1990. Subjects were randomized to receive either oral amoxicillin for 10 days or placebo. Tests for antibodies to *B. burgdorferi* (EIA) were performed serially for three months. Ticks were tested for evidence of infection with *B. burgdorferi* using PCR. Antibiotic compliance was measured with a urine bioassay. Subjects were observed for one year for clinical evidence of Lyme disease. No seroconversions were observed. None of the 120 treated subjects developed clinical evidence of Lyme disease. One (0.9%) of the 110 subjects in the placebo group developed clinical evidence of Lyme disease (erythema migrans). Nobody in the placebo group and 56% in the treatment group had antimicrobial activity in their urine on day seven. Twenty percent of *I. dammini* removed from each group (treatment and placebo) were positive for infection with *B. burgdorferi*. NOTE: This was a follow-up study to Gerber *et al.* (1990), described above. The authors recently provided CDC with the following additional information: of the 204 identifiable ticks, 141 (69%) were nymphs, 43 (21%) were adults, and 20 (10%) were larvae. Thirteen percent of nymphs, 35% of adults, and no larvae were positive for infection with *B. burgdorferi*.

In addition, CDC is aware of at least one other ongoing epidemiologic study of this issue, a randomized double-blinded placebo-controlled clinical trial by Dr. Tom Sell and colleagues at the Marshfield Clinic in Marshfield, Wisconsin. Subjects who present with attached ticks are randomized to receive either three days of oral minocycline or placebo. Ticks are examined for the presence of spirochetes using an indirect immunofluorescence assay. The following are preliminary results as of August, 1991: enrollment of 173 subjects, 85.7% of the ticks submitted were *I. dammini*, similar rates of infection (about 18%) were found in *I. dammini* removed from each of the two groups (treatment and placebo), and no development of clinical evidence of Lyme disease in any subject.

COMMENT: These studies highlight the relatively low risk of infection and disease arising from a recognized tick bite in an endemic area. The principal factor that would seem to explain the low apparent risk of infection is that transmission is probably inefficient in the first 36-48 hours of tick attachment.[5-6] Attached ticks which are removed are less likely to have transmitted infection than are ticks that are not noticed. Only about 30% of persons with early Lyme disease remember having been bitten by ticks in a four-week period prior to onset of symptoms.[7] Engorged infected ticks have the highest probability of transmission of *B. burgdorferi* to humans, and yet a substantial majority of these apparently have not produced infection at the time of removal (Nadelman *et al.* 1990, above). The incidence of transmission of *B. burgdorferi* by a recognized *I. dammini* bite in an endemic area may be no higher than the incidence of adverse effects from a standard course of antibiotics.[2] If it can be shown to be effective and safe, single dose prophylaxis may be a reasonable alternative to no prophylaxis at all.

All of the above epidemiologic studies were done in the northwestern or north central United States where *I. dammini* is the vector of Lyme disease. The risk of transmission from a recognized bite by *Ixodes pacificus*, the vector on the West coast, is unknown. If prophylactic antibiotics are not routinely indicated in areas where *I. dammini* occurs (and where typically 20-80% of nymphs or adults of this species are infected with *B. burgdorferi*), their use is probably even less warranted in the West, where typically only 1-3% of nymphal or adult *I. pacificus* are infected.

When consulted by health care providers, CDC/DVBID staff do not currently recommend the routine administration of antibiotics to prevent Lyme disease following a known tick bite. The CDC does promote primary prevention with the following approach:

- persons should be aware of and, if possible, avoid areas likely to be infested with disease-bearing ticks,
- persons in tick-infested areas should take personal protective measures, such as wearing of proper clothing, use of repellants and contact acaricides, and frequent inspection for ticks on clothing and body surfaces so that ticks can be detected and removed promptly.

Secondary prevention can be achieved by educating care providers and the public to quickly recognize the signs and symptoms of Lyme disease, and on the need to promptly diagnose and treat the disease should it occur.

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The Art Long, Judgment Difficult*

JAY KATZ, M.D.

THIS day, the beginning of your medical school education, must be one of great expectation and considerable anxiety. I join you in your anxiety; for I have never had the opportunity to address an incoming medical school class. During the last few weeks I asked myself: What can I convey to you—my young, soon-to-be fellow doctors—on this momentous occasion that has meaning and that you will remember?

Perhaps you will remember what I remember about my early years as a medical student. Thus, let me tell you a few stories about my past and their implications for my, and I hope your, education as physicians.

I entered medical school at the end of World War II. Those were great years for medicine. We were not beleaguered, as you are, by cost containment or government regulations; we were not accused of charging too much, of practicing impersonal technological medicine. We wielded considerable authority; nobody questioned our authority to superintend, according to our professional judgment, the medical fate of our patients and society.

Much has changed, but even though our authority as physicians is now being questioned, you will continue to be esteemed, even revered; for when sick, and thus beset by existential anxiety, patients wish to trust you, surrender to you, find in you a gentle guide who will return them to health or ferry them caringly across the river Styx.

In the waning years of the twentieth century you have new opportunities, as we had at the end of a terrible war, to bring glory to a profession which I hope you will love as much as I do. I shall return to this point at the very end of this address.

On my first day of medical school, I sat in the anatomy lecture room, anxious and trembling. "Would I measure up, would I make it?" I did and so will you. National Board exams are monsters; they ought to be thoroughly revised, but young women and men can defeat monsters not only in fairy tales but in life as well, and you will too. Remember these words two years hence when you study for these exams.

To return to the anatomy lecture room: In strode Dr. Robert Montreville Green, a descendant of generations of Harvard Medical School professors. He was dapperly dressed, in command of the situation. He walked to the other end of the platform. There stood a stretcher, draped by a white sheet, which in my anxiety I had not noticed. He majestically removed the white sheet and exposed to view a corpse. He turned around and spoke these, his first, words: "Doctors (he always called us doctors), for the next five months I shall begin to teach you how to defeat your great enemy: death."

And this is what he tried to do. I admired Dr. Green because he taught us principles of anatomy, not the minutiae of Gray's *Anatomy*. However, his opening words should have been different and our first medical encounter should not have been with a corpse. Dr. Green, alone on the platform, would have been sufficient; if anyone else needed to be there, it should have been a living patient. Death, my young colleagues, is not your enemy who needs to be defeated. Death challenges our professional sense of omnipotence and as you will soon learn, as you observe your elders, physicians have an inordinately overgrown sense of their omnipotence. However defensive, it permeates their conduct.

We physicians experience great difficulty in accepting our impotence in the face of disease and inevitable death. The enemy is our inability to accept the limits of what we can do, to accept that we are not omniscient, omnipotent. We are not gods. Remember that our great ancestor, Asclepius, was only half-god. He was also half-man, perhaps out of recognition that while our patients will at times view us as gods, and in turn so will we view ourselves, we should remember that ultimately we are mortals, linked to our patients as fellow perishable human beings.

JAY KATZ, M.D., Elizabeth K. Dollard, Professor of Law, Medicine, and Psychiatry, Yale Law School, New Haven.

* Convocation Address for the Medical and Dental Classes of 1995, University of Connecticut, School of Medicine, 26 August 1991.

I learned this lesson two years later, during the summer between my second and third year of medical school, when I served as a sub-intern at Kings County Hospital in Brooklyn. I was assigned an elderly patient who was dying of cancer. My resident told me that he had only a few days to live. I kept him alive for weeks and I was so proud. My resident was amazed and he praised me for my dedication which had made me persist in removing again and again fluid from his abdomen, finding veins that had not collapsed so that I could nourish and sustain him. I stuck him with needles, barely noticing his pain. He did not complain, probably he was touched by the sincerity of my efforts; perhaps he did not want to hurt me.

However, one day he could no longer contain himself; could not suppress his pain and anger; and he sharply reprimanded me: "You are hurting me too much, stop, let me die in peace." I was stunned and at first retreated. "What ungratefulness; does he not appreciate what I am doing for him?" However, I went back and we started to talk. He told me that he knew his days were numbered, that he had said good-bye to his family, that he was sorry that his life was coming to an end, but that he was ready to die. A few days more did not matter. The pain of staying alive was too unbearable. I packed up my needles and for the next few days my words, and I hope caring presence, meant much to him. He, as patients can be, if we listen to them, was one of my great teachers.

During my second year of medical school, we were given our one lecture on the care of the patient. That, in those days, was considered sufficient. Dr. Conrad Wesselhoeft, Jr., another descendent of Harvard Medical School professors on both sides of his family, ended that lecture with a story about his first week as an intern, assigned to the emergency room. That same week he had joined his parents and siblings for dinner. With great excitement he told them about a young man who had come to the emergency room with moderately severe abdominal pain. Conrad Junior had examined him and diagnosed "acute appendicitis." He, of course, recommended immediate surgery, but his patient pleaded with him to delay the operation for a few hours because of an important, most crucial, business appointment. Conrad acceded to his request. The patient returned, the operation was successfully performed and Conrad had been first assistant at the operation. All was well that ended so well.

As Conrad Junior related his story, Conrad Senior looked sterner and sterner. He said nothing and his demeanor indicated to his family that he did not want anyone to talk. The rest of the meal was eaten in unaccustomed utter silence. After coffee and desert, Conrad Senior got up, turned to his son and said "Come to my study." There he berated him for having abdicated his professional responsibility to his patient by allowing him to leave. He chided him for his inexcusable conduct of which his son surely could not be proud. Conrad Junior ended the lecture by merely saying that he had learned an important lesson. He did not tell us, however, what he had learned.

When years later I remembered the lecture, I began to wonder: "What was the lesson he had learned?" That he should have made it virtually impossible for his patient to leave? Doctors have ways of doing so by exaggerating the seriousness of the situation beyond its seriousness and thus tying down patients not with chains but with ominous words. Yes, this was a serious situation. Conrad should perhaps have said more than he did, have impressed on his patient the dangers of waiting. However, in my view the ultimate decision was for his patient to make. Young Conrad had before him not only a patient but also a person and both deserved respect.

You will frequently be in Conrad Junior's shoes when confronted with patients suffering, for example, from cancer, hypertension, and angina whom you can treat in a variety of ways and where the decision whether and how to treat depends not only on what medical science, but also the art of medicine, might dictate. And by art I mean here consideration of the wishes of the person with respect to quality of life.

What, on reflection, I have learned from the encounter between Conrad Junior and Conrad Senior is not that one or the other was right or wrong, but that both should have talked about the complexity of decision making in the practice of medicine. My young colleagues, learn to resist the temptation in all your future encounters with patients to find easy answers, and question, at least silently, the easy answers which some of your elders will espouse. To practice our profession requires wisdom and the first lesson to be learned about medical wisdom is this: that certainty eludes us. Of course, the treatment of choice for acute appendicitis is immediate surgery, but not always.

In today's world, as you will soon learn, we also try to find certainty by succumbing to our inordinate fear of malpractice suits. "What if the appendix bursts, will we then be confronted with the charge of malpractice?" Perhaps; and this is another complex problem about which you will learn a great deal from professor Jay Healey. But let me say only in passing that, such legal threats notwithstanding, we must not lose sight of our professional obligations to our patients and must not surrender to laws if they compel us to violate our professional duties. And to make matters more complex: Our fear of malpractice suits may be self-serving, for it permits us to seek reinforcement of our own authoritarianism from the authoritarianism of law. Therefore, our first task is to remain true to our professional commitments.

Yet, the question which the story of young Conrad so compellingly raises is this: "What are our professional obligations to our patients?" You must ponder this question throughout your professional lives. In doing so, remember Hamlet's words: "There are more things between heaven and earth, Horatio, than are dreamt of in your philosophy."[1]

One final story, from later in my professional life, about a 21-year-old, single woman whom I first met at a panel discussion on the treatment of breast cancer. I have written about her in my book, *The Silent World of Doctor and Patient*,[2] in which I argued for greater participation of patients in medical decision making. I called the young woman Iphigenia Jones. Giving her a most common surname and a most uncommon first name—except for those familiar with Greek mythology—underscores both the frequency of the event and the rarity of what ultimately transpired, including the fact that, like her Greek sister, her sacrifice too was barely averted.

Some time before the panel discussion she had discovered a lump in her breast. Biopsy revealed a malignant lesion. She agreed to a mastectomy, with the extent of the surgery to be determined by what her doctor would discover during the operation. Her surgeon, who participated in the panel discussion, related to the audience his increasing doubts, as the morning of the surgery drew closer, about whether to proceed without first disclosing to Iphigenia the availability of alternative treatments, particularly radiation therapy. He had not spoken to her about alternatives because he firmly believed that surgery was the best treatment for her and that all alternatives were inferior.

Only his misgivings about having to perform such a mutilating procedure on a person that young and attractive led him to consider telling her about alternative treatments, even though such therapies were employed by other physicians at his own medical center. On the evening prior to the operation, his concerns about having remained silent, concerns that he did not fully understand, became so insistent that he returned to the hospital. He told her that, although he believed surgery to be without question the treatment of choice, alternative treatments existed and that he wished to acquaint her with them if she so desired. He added that he was not sure whether he was doing the right thing in discussing such matters with her, but he felt compelled to confide in her. Pascal had put it well: "The heart has its reasons which reason knows nothing of."[3]

They talked for a long time. Iphigenia decided that very night to postpone surgery for a few days, to consult other doctors, and then to make a choice. Eventually she opted for a lumpectomy (excision limited to the tumor mass) and radiation therapy. At the panel discussion she spoke knowledgeably and intelligently about the risks she had taken, and movingly about her impending marriage, especially her great joy over now being able to begin life with her beloved physically unscarred.

The discussion from the floor was heated and rife with controversy. Physicians defended their favorite therapies and questioned, if not attacked, other therapeutic approaches to the treatment of breast cancer. They were almost completely united on only one proposition: "It is irrational to allow patients to make these decisions." Despite Iphigenia's testimony, some asked, though the questions suggested the answer: "If doctors have such trouble deciding which treatment is best, how can patients decide? Are not patients' interests better served by trusting submission to their doctors' authority?" The physicians did not clarify the one crucial word, "best," and the senses in which they employed it.

Iphigenia's story illustrates physicians' doubts about inviting patients' participation in a decision that will deeply and irrevocably affect their future welfare in very personal ways. From doctors' points of view, since patients cannot be trusted to comprehend medicine's esoteric knowledge sufficiently well, such an invitation does not make sense. Doctors believe that patients are protected far better if they trust their doctors' authority and have confidence in their altruistic dedication.

However, the extent to which patients can understand medical knowledge is at least an open question. Physicians have had too little experience communicating their esoteric knowledge to patients to permit any conclusive answers. Beyond assertions that patients in order to understand must be given a minicourse in medicine, the literature has not seriously addressed the question: Is esoteric knowledge a serious handicap to disclosure and consent, when an effort is made to explain it?

The esoteric knowledge excuse has been employed sweepingly in order to keep silent about the simplest as well as the most complicated medical interventions. Iphigenia, about this I have few doubts, learned a great deal about the treatment of breast cancer and the consequences of whatever therapy she would finally select. Her experience alone should begin to cast doubt on the categorical assertion that any given patient is unable to sort out with her doctors which treatment suits *her* needs best.

The consequences to Iphigenia of either a mastectomy, perhaps a radical one, or a lumpectomy, with or without radiation treatment, were fateful. All were treatment modalities that physicians at the hospital to which she had trustingly come were prepared to advocate as appropriate interventions. Would silence about their availability have been a preferred alternative? Should Iphigenia have placed complete trust in her surgeon's dedication to her welfare and let him decide on her behalf?

What was in Iphigenia's best interest, I submit to you, could only be discovered by conversing with her, yet many of the doctors who discussed her case thought this was not an appropriate inquiry. Since chance determined the first choice she had made of a physician, should chance have decided Iphigenia's fate? Does trust command silence?

I apologize that on this, your first, day I have said so much about the complexities of your future life. However, I would have been unfaithful to you and myself had I not spoken as I did. My love of our profession precluded my doing otherwise.

In conclusion, let me quote the final words of Francis Peabody, another Harvard Medical School professor. In his celebrated lecture on "The Care of the Patient" he uttered these moving words:

> [t]he good physician knows his patients through and through, and his knowledge is bought dearly. Time, sympathy, and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.[4]

I have reflected on this passage over many years. Once I wrote that Peabody left the secret unrevealed. Now I believe that I know what he tried to convey to us by asking us to know our patients and exhorting us to be humane.

The task of knowing our "patients through and through" is an impossible one and should not even be attempted. We can get to know our patients only to a limited extent. Yet, by changing one word in his last sentence the secret of how to care for the patient became clear to me: "the secret of the care of the patient is in caring for the *person*." We of course bring our esoteric knowledge to our medical recommendations, but we must then not only see the patient but also the person before us. We must learn to listen to the person in the patient before deciding jointly what course of action to follow.

This brings me full circle to the beginning of this address. Your task, in the light of governmental regulations of our profession is to form a new, unaccustomed alliance with your patients. They and you, as citizens of a democratic society, can then demand that any regulations will not compromise the health needs of the individuals who have entrusted themselves to your care. We cannot do it alone, we must learn to join forces with an aroused public, particularly with our patients.

Hippocrates once said this about the practice of medicine: "Life is short, the Art long, Opportunity fleeting, Experiment treacherous, Judgment difficult."[5] Remember these words, for our profession is a hard task master. I congratulate you, my colleagues, on the choice you have made. No other profession is ultimately as rewarding as is the one you have chosen. Accept my hopes for you and my best wishes for a long, rewarding personal and professional life.

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Discoveries

Lynn M. Cleary, M.D.

ABIGAIL found the moon last night.

It was a quiet discovery, like most of hers have been. I, on the other hand, heard an orchestra. These are secular miracles to me, her realizations. This one was especially magical because it was so unexpected. Yesterday was full-tilt, non stop. I finally left the hospital after a late admission and went to pick her up at her grandmother's house; it was quarter till ten when I arrived, and she hadn't been able to fall asleep in her portable crib. She was edgy, of course, as if she resented the fact that I'd left her all day but the same time resented my intrusion at returning; she'd had her grandmother's undivided attention. Once we were outside she was quiet, attentive. The air was clear and cold, the moon was almost full, and it was surprisingly bright out with all the snow. She pointed up and said, "Deesh?" stared for a moment, then looked at me and smiled with the unmistakable delight of making a connection. All those hours of reading *Good Night, Moon* somehow fit together with her ability to select and then point to something and finally to show me what she had found. We both rode that wave for miles on the way home. Her car seat was near the window, so she could look out and contemplate her discovery. She was quite content with it, checking for its presence at intervals and then just resting or humming with the sound of the motor. The last few miles were along the lake, where the moon's reflection was so lovely. We were both quiet then.

Much of the time my emotions are so private that I'm not certain of them, but motherhood has articulated very clear feelings. I am happy to be feeling what millions of mothers feel, what my mother and grandmother and sister have felt. Part of being a new mother is essentially instinctive, connecting me to ancestors and descendants. Another part is having body and emotions merge, as when milk stains my shirt when she cries. It is hard to describe what it is like to be kicked from the inside out, to nurse, to cry instinctively when she is in pain. I quite like this intimacy.

Motherhood has been remarkable in so many ways; I am only beginning to learn of its effect on me as a physician. It is not just being a patient, going through labor and delivery, healing wounds, or putting up with hemorrhoids. Nor is it learning how to nurse together, mix formula, or figure out if the baby has otitis media. Something in my brain is connecting differently now. Like Abigail, I find things right in front of me that may have been there all along. My neurons are redirected by hormones, my sensibilities have different receptors—more of some, less of others, perhaps new ones. It is not a new language or a different culture, and it is more than a simple renewal.

I have begun to sense that dimension of a patient-doctor relationship that relates to giving in a different way. Traditionally, one thinks of a patient receiving a diagnosis, information, treatment, of a doctor giving care, time, advice. I have been uncomfortable receiving gifts from patients; it was different receiving their gifts as a mother. I must feel motherhood is different from my other roles with them, perhaps more comfortable, perhaps more deserving. Maybe it is the nature of the gifts that made it easy. I have sensed the strength of good feeling when they gave me a blanket, or a rattle, or a bib. Giving gifts empowers the giver, and the usual doctor-patient relationship empowers the doctor in that way. As physicians we assume that power, usually with good intentions, but it does shift the fulcrum of the relationship. It feels very right to respond to their inquiry about my family, to spend the time sharing that gift of affection. Somehow my child has helped me realize and accept a very important dimension to patient-doctor relationships, before she can even talk.

Another of her silent instructions is to appreciate time. She is my little yardstick, measuring off days and months with each new pound, new skill, new tooth. I am better organized and seem to accomplish more in less time. No doubt there are other ways to learn these skills, but motherhood does hasten their acquisition. Cooking and holding the baby at one time, reading while nursing her—these are good exercises and readily transferable to reading abstracts between returning phone calls at work or eating a sandwich while waiting for the file room clerk to

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find an x-ray. Although doing two things at once is often necessary at work, it feels more natural now and less of an imposition.

I am also learning to let circumstances direct me. Life is so much easier if I let her show me how she can untie her shoes rather than insisting she keep them on, and much more fun when she chooses between the tambourine and castanets than when I try to teach her a tune on the xylophone. It matters less what antibiotic the resident chooses for treating the pneumonia than that he or she decided to admit the patient for care in the first place at two o'clock in the morning. If Mr. Smith chooses to talk to me about his car mileage and snow tires, why should my own poor sense of timing force him to discuss his wife's terminal cancer that day? There is time for direction and a time for appreciation. My daughter is helping me sense the difference.

Not long after returning from maternity leave, one of my patients entered the terminal stage of a prolonged illness. She and her husband had been patients for several years, and we had all been aware of the inevitable. Nonetheless, each dying process is a little different, each family circumstance unique. Most physicians process death objectively (write the DNR order, be sure the morphine drip is adequate), but most also occasionally find it jarring, sometimes even unacceptable. This woman's terminal illness was uncomfortable for me. Perhaps it was the juxtaposition of my daughter's recent birth with this patient's impending death, my identification with her as a mother and grandmother,with them as loving parents. It may have been her stoicism, the unfairness of all her suffering.

We were able to have the hospice become involved in her terminal care. During the initial interview among family members, hospice staff members, and me, her husband asked specific questions about how she would die. They were good questions, hard ones to answer, but one of the answers from the hospice in-patient coordinator hit home for me. She explained that patients labor before they die, just as women labor before giving birth. This patient had been laboring. She had sensed the process and was proceeding with an inner direction. "Don't fight," recommends the labor coach in the birthing classes. Somehow, this process of dying became less uncomfortable for me, and, I think, for the family. The patient had just celebrated a 75th birthday the week before entering real labor. She was ready to labor at the other end of her life. It was less a concept of her leaving than a natural transition from one place to another. The notion of hospice staff working as labor coaches seemed ridiculous, but oddly appropriate, sort of like whiskey and laughter at an Irish wake. No doubt the next of my patients to die will be very different, another disease, a different family. But the concept of laboring as part of dying will now be part of my framework to deal with it.

Motherhood shares so much with the practice of medicine; as Osler described the latter, it is "a way of life." It will be part of my awareness now, an inseparable part of my medical experience. No doubt little Abigail will show me the sun, the stars, and the planets some day.

Support Group for Persons Newly Diagnosed with Multiple Sclerosis

The Greater Connecticut Chapter of the National Multiple Sclerosis Society is sponsoring a support group for people who are newly diagnosed with Multiple Sclerosis within the past two years. Spouses, significant others, and family members are welcome. The group will meet at the University of Connecticut Health Center, Academic Entrance, Farmington, beginning 3 December, from 7-8:30 pm. Meetings will be on the first and third Tuesday evenings of the month through May 1992. Topics will include such issues as Physical Management of Symptoms and Psychosocial Coping.

It is necessary to register. Anyone interested should write or call Tina Grant, Chapter Services Associate, Greater Connecticut Chapter, National Multiple Sclerosis Society, 74 Batterson Park Road, Farmington, 06032, 674-1995.

Narcotic Analgesics in Renal Failure

JILL FITZGERALD, PHARM.D.

Introduction

PAIN management in patients with renal failure is a frequently encountered problem in clinical practice. As with most medications, clinical studies and preliminary pharmacokinetic analysis exclude patients with varying degrees of renal dysfunction. Although certain dosing strategies can be employed for patients with renal dysfunction according to the drug's elimination characteristics, oftentimes it is not until the drug has been used in a large number of patients that certain adverse events are noted. This is particularly true for narcotic analgesics in renal failure. In addition to the pharmacokinetic differences between patients with normal renal function and those with renal failure, pharmacodynamic differences may also be present and are more difficult to evaluate.

Clinical and pharmacokinetic studies, case reports, and clinical experiences will be utilized to categorize the safety of narcotic analgesic use in renal failure patients (Table 1).

Narcotic Analgesics to Avoid in Patients with Renal Failure

Meperidine (Demerol) — Szeto et al[1] studied the pharmacokinetics of meperidine and its active metabolite, normeperidine after multiple doses in seven end-stage renal disease (ESRD) patients and seven cancer patients with normal renal function. They reported two patients with renal failure who developed signs of central nervous system (CNS) excitation manifested by irritability and twitching in one patient and gradual agitation, confusion, and seizures in the other. Measurement of plasma levels of meperidine and normeperidine one hour after the last dose was determined for each patient. Patients with renal failure had significantly higher concentrations of normeperidine and a higher normeperidine/meperidine ratio than patients with normal renal function. In addition, the concentration of meperidine was significantly lower in patients with renal failure but may reflect the lower dosage of meperidine used in ESRD patients. These data suggest that, on chronic dosing, normeperidine accumulates to a significant degree in patients with renal failure. The half-life of normeperidine was calculated in two cancer patients with normal renal function to be 14.2 hours and 20.9 hours as compared to 34.4 hours in one renal failure patient.

These data have important clinical significance since it has been shown that in animals normeperidine is approximately two to three times more toxic than meperidine. Toxicity is manifested by CNS excitation, convulsions, and respiratory depression. Normeperidine has greater CNS stimulatory effects while meperidine has greater CNS depressant effects. These opposing effects become more significant with chronic dosing in patients with renal failure; a higher normeperidine/meperidine ratio favors CNS excitation. In addition, animal studies have demonstrated that naloxone administration has reversed the depressant effects of meperidine (respiratory depression) but not the CNS excitatory effects of normeperidine (convulsions).[2-4] It appears that the normeperidine concentration, duration of use, total dose, and the normeperidine/meperidine ratio are all related to the toxicity of meperidine in renal failure.

Propoxyphene (Darvon) — After oral administration, propoxyphene undergoes significant first pass metabolism in the liver and only a small fraction of the parent compound appears in the serum. The remainder is N-demethylated to norpropoxyphene which is subsequently eliminated in the urine. Norpropoxyphene has a longer elimination than propoxyphene in normal patients and, therefore, accumulates on chronic dosing. Like propoxyphene, norpropoxyphene also has cardiac depressant effects and is thought to contribute to propoxyphene's toxicity in overdose. Because nor–propoxyphene is primarily eliminated by the kidney, it is

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Table 1

Safety Classification of Narcotics in Renal Failure

Avoid in Renal Failure
meperidine (Demerol®)
propoxyphene (Darvon®)

Use with Caution in Renal Failure
morphine
codeine
dihydrocodeine (Synalgos-DC®)
oxycodone (Tylox®, Percodan®, Percocet®)
methadone (Dolophine®)

Suggested as Safe in Renal Failure
buprenorphine (Buprenex®)
hydromorphone (Dilaudid®)

thought to affect significantly the toxicity of propoxyphene in renal failure patients. To determine the effects of renal failure on the disposition of propoxyphene and norpropoxyphene, the pharmacokinetics of propoxyphene were studied in seven anephric patients and seven healthy subjects following a single 130 mg oral dose.[5]

It was determined that the peak concentration of both propoxyphene and norpropoxyphene were significantly higher in anephric patients than in normal subjects. Furthermore, the half-life of norpropoxyphene is prolonged while that of propoxyphene is essentially unchanged in anephric patients. This suggests that on multiple dosing, norpropoxyphene will accumulate and can lead to respiratory and cardiac toxicity. Naloxone is effective in reversing the respiratory depressant effects of propoxyphene but not its cardiac depressant effects. In addition, propoxyphene and norpropoxyphene are not significantly removed from serum by hemodialysis.[6]

Narcotic Analgesics to Use with Caution in Renal Failure

Morphine — There have been several case reports in the literature suggesting that patients with renal failure are more susceptible to the analgesic and adverse effects of morphine with significant respiratory depression being reported.[7-9] Morphine is metabolized in the liver to two major metabolites: morphine-3-glucuronide (M-3-G) and morphine-6-glucuronide (M-6-G). Both metabolites are excreted in the urine. M-3-G is an inactive metabolite whereas M-6-G is active and more potent than morphine.[10-12] Previous studies of morphine pharmacokinetics in renal failure have used an RIA assay which included measurement of M-3-G and M-6-G. It was proposed that morphine was accumulating in renal failure rather than the metabolites. With the separation of morphine from its metabolites using high performance liquid chromatography (HPLC) analysis, it is now thought that the prolonged narcosis from morphine is secondary to accumulation of the M-6-G metabolite.

Osborn et al in a series of three patients with renal failure and prolonged respiratory depression, were able to measure concentrations of metabolites in plasma when there was little or no morphine measurable.[7] As the concentration of M-6-G declined, the toxicity reversed. The calculated half-life of M-6-G ranged from 38-103 hours suggesting significant accumulation in these patients.

Dihydrocodeine and Codeine — Very little is known about the disposition of dihydrocodeine in patients with normal renal function. It has been proposed that it undergoes hepatic metabolism to glucuronidated, N-demethylated and O-demethylated metabolites.[13] Its metabolic fate has not been determined in patients with renal failure. Case reports of prolonged narcosis from dihydrocodeine in patients with renal failure have been reported.[14,15] Upon oral administration in patients with renal failure, higher peak dihydrocodeine concentrations and increased area under the curve (AUC) were reported in comparison to patients with normal renal function.[16] Several theories on its pharmacokinetics and pharmacodynamics in renal failure have been postulated including increased systemic bioavailability due to decreased first-pass hepatic metabolism, increased patient sensitivity to narcotic analgesics, decreased renal clearance or hepatic metabolism of dihydrocodeine or one of its metabolites.[17] Further study is needed to define the mechanism.

Codeine has been reported to cause prolonged narcosis in patients with renal failure.[18,19] In patients with normal renal function, codeine is metabolized in the liver to codeine-6-glucuronide, norcodeine, and morphine. Norcodeine is an active and equipotent metabolite.[17] Guay et al determined that the renal clearance of codeine was significantly lower and the half-life significantly longer in patients with ESRD and on hemodialysis following single IV and oral doses of codeine.[20] This suggests the potential for significant accumulation on chronic dosing. In fact, based on their data, toxic steady state concentrations of codeine would have been achievable in four of the six patients studied following a suggested dose of 60 mg orally every six hours.

The renal clearance of the metabolites (codeine glucuronide, morphine, and morphine glucuronide) was significantly lower in patients with ESRD. Half-lives were not assessed and a differentiation between M-6-G and M-3-G could not be made. Therefore, it is not possible to speculate on the accumulation of these metabolites. Altered patient sensitivity, decreased renal elimination of parent drug and metabolites, and enhanced effect secondary to hypocalcemia have all been proposed mechanisms of the prolonged narcosis secondary to codeine in patients with renal failure.[19,20]

Oxycodone — Oxycodone is metabolized to noroxycodone, conjugated oxycodone, oxymorphone, and conjugated oxymorphone. The only known active metabolite is oxymorphone. Although, to our knowledge, oxycodone has not been reported as causing unusual adverse effects in patients with renal failure we have had some problems with CNS toxicity and sedation with usual doses in this patient population. The relative risk of toxicity is probably low, however, high doses over short periods of time must be used with caution.

Methadone — Both hepatic and renal elimination of methadone are important in its elimination. Following a single oral dose of 15 mg, 21% is excreted in the urine unchanged, 30% is excreted as the metabolite 2-ethyl-1-5-methyl-3, 3-diphenyl-1-pyrroline and 1% as 2-ethyl-5-methyl-3, 3-diphenyl-1-pyrroline. Both metabolites are pharmacologically inactive. On chronic dosing, there is a 3-fold increase in the excretion of metabolites suggesting enhanced metabolism.[21]

Kreen et al described two patients with chronic renal failure on maintenance methadone treatment.[22] They found that plasma methadone concentrations were within the normal range in both patients and that 98% of the dose was recovered in the feces as the 2-ethyl-1-5-methyl-3, 3-diphenyl-1-pyrroline metabolite in the anephric patient on hemodialysis. However, the second patient who presented with obtundation had ESRD requiring peritoneal dialysis. His fecal elimination of the drug accounted for only 15% of the dose. The authors state that there was a significant amount of methadone and metabolites excreted in the urine but specific values were not reported. Further study is necessary to determine the pharmacokinetics and pharmacodynamics of methadone in renal failure patients; however, a shift in elimination from urinary to fecal may occur in anephric patients. Because of its long half-life, accumulation of methadone can occur in any patient, therefore, careful dosage titration should be employed regardless of renal function.

Narcotic Analgesics Suggested as Safe in Renal Failure

Buprenorphine — Buprenorphine is an opioid partial agonist analgesic which is metabolized to two metabolites; buprenorphine-3-glucuronide and norbuprenorphine. Approximately 70% of an oral or IV dose is excreted in the feces as unchanged drug.[23] In rats, buprenorphine-3-glucuronide is inactive as an analgesic where norbuprenorphine is 40 times less potent than the parent drug. Hand et al studied the pharmacokinetics of buprenorphine after single dose and continuous infusion in patients with renal failure and normal renal function.[24] Following a single 0.3 mg buprenorphine IV dose, the elimination half-lives were not significantly different between the two groups and buprenorphine metabolites were not detected in plasma.

During continuous infusion of buprenorphine, the clearance of parent drug was similar and there was no significant accumulation of buprenorphine in either patient group. Patients with renal failure accumulated the buprenorphine-3-glucuronide and norbuprenorphine metabolites 15 and four times greater, respectively, than patients with normal renal function. Infusions were titrated to achieve sedation in mechanically ventilated patients. There were no reported adverse effects in either patient group.

Accumulation of the inactive buprenorphine-3-glucuronide and active but much less potent norbuprenorphine does occur with chronic dosing of buprenorphine but not to a clinically significant degree. As a class, the opioid partial agonists are generally not used for chronic pain syndromes as they are limited by a ceiling analgesic effect and therefore it is not useful to titrate them over a wide dosage range.

Hydromorphone — Hydromorphone is eliminated by both hepatic and renal routes. It is presumably conjugated with glucuronide and reduced to 6-a and 6-ß hydroxyhydromorphone. In normal healthy volunteers, approximately 43.5% of the dose is excreted in the urine primarily as conjugated hydromorphone (35%), free hydromorphone (6%), and small amounts of both 6-a and 6-ß hydroxyhydromorphone.[25] Other routes of elimination have not been investigated. The hydroxymetabolites are less potent analgesics than hydromorphone. The activity of the glucuronide is not known.

To our knowledge, there have been no reported cases of prolonged narcosis in renal failure patients secondary to hydromorphone reported in the literature and no pharmacokinetic studies have been performed in patients with renal failure. The Pain Control service at Hartford Hospital has used hydromorphone in patients with ESRD on dialysis as well as patients with renal insufficiency with good results and seemingly no increase in toxicity.

Conclusion

Classification of the safety of narcotics in renal failure is very difficult because of a large interpatient variability in sensitivity to narcotic analgesics. However, with the availability of excellent alternative narcotics, meperidine and propoxyphene should be avoided in this patient population. Buprenorphine and hydromorphone appear to be the safest narcotics in renal failure and have been used frequently and safely in patients with ESRD and renal insufficiency at our institution.

Morphine, codeine, dihydrocodeine, oxycodone, and methadone should be used with caution in renal failure. Although not all patients will have problems with these narcotics, patients should be observed for signs of toxicity and sedation. Moderate dosages for short periods of time should pose minimal risk.

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Rapid Diagnostic Tests for Group A Streptococcal Pharyngitis

THE MEDICAL LETTER

ANTIBIOTIC treatment of group A streptococcal pharyngitis can relieve symptoms, limit transmission of infection, and prevent suppurative and nonsuppurative sequelae. Clinical findings may be unreliable, however, in establishing the diagnosis, and conventional throat cultures take overnight or longer to produce results. Rapid office tests for streptococcal pharyngitis can make the diagnosis in about 10 minutes. Since the previous *Medical Letter* article on this subject (*Medical Letter* 1985; 27:49), many new tests have been marketed, including some that use new technologies.

RAPID TEST KITS — Some of the diagnostic tests now marketed in the USA that claim to detect group A streptococcal antigens directly from a swab of the patient's pharynx are listed in the table. Most test kits include reagents for extraction of the antigen from a dacron- or rayon-tipped swab and the antibodies needed to visualize the extracted antigen. Extracted antigen is detectable by observing either agglutination of antibody-coated latex particles or a color change due to an enzymatic reaction (ELISA) or to colored lipid, colloid, or latex particles binding to antibody. In general, colorimet-

Some Rapid Tests for Group A Streptococci

Manufacturer	Test	Detection Method	Cost[1]
Abbott Diagnostics	*TestPack Plus Strep A*[2,3]	Colorimetric: colloid	$ 3.95
ADI Diagnostics	*Visuwell*[4]	Colorimetric: ELISA	2.08
Antibodies Inc.	*Detect-A-Strep*	Agglutination	2.00
Becton Dickinson	*Culturette*[3,5]	Agglutination	2.73
Becton Dickinson	*Directigen 1-2-3*[3,6]	Colorimetric: liposome	3.75
Becton Dickinson	*Q Test Strep*[7]	Colorimetric: liposome	3.75
Diagnostic Products	*Patho-Dx Strep A*	Agglutination	1.79
Difco	*Strep A-CUBE*	Colorimetric: ELISA	3.50
Hybritech	*Concise Strep A*	Colorimetric: latex	4.10
Hybritech	*ICON Strep A*[3,8]	Colorimetric: ELISA	3.90
Kodak	*SureCell Strep A*	Colorimetric: ELISA	3.85
Leeco Diagnostics	*Preview Strep A*	Colorimetric: ELISA	3.50
Medical Technology	*Optitec Strep A*	Colorimetric: ELISA	2.90
New Horizons	*Smart*[9]	Colorimetric: colloidal gold	3.75
Pacific Biotech	*Cards Strep A*[3,10]	Colorimetric: ELISA	3.60
Pacific Biotech	*Cards O.S. Strep A*	Colorimetric: latex	4.20
Unipath	*Clearview Strep A*	Colorimetric: latex	3.25
Ventrex	*Ventrescreen Strep A*[3,11]	Colorimetric: ELISA	2.40
Wellcome Diagnostics	*Reveal Colour Strep A*[3]	Agglutination (colored beads)	2.20

1. Per test to the laboratory
2. P Egger et al, Eur J Pediatr, 149:256, 1990
3. CB White, J Pediatr, 113:691, 1988; S Hoffman, Diagn Microbiol Infect Dis, 13:209, 1990
4. J-M Chu et al, Acta Paediatr Sin, 31:151, 1990
5. B Taubman et al, Am J Dis Child, 143:102, 1989
6. BD Reed et al, Arch Intern Med, 150:1727, 1990
7. MA Gerber et al, J Clin Microbiol, 28:1463, 1990
8. Also assembled and distributed by Baker Diagnostics as *Confident PLUS*
9. Requires only a few steps but, according to Medical Letter consultants, reaction may be faint and difficult to read.
10. RJ Manasse, J Clin Microbiol, 27:1657, 1989
11. M Hasin and A Furst, J R Coll Gen Pract, 39:332, 1989

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ric end-points are easier to read than agglutination reactions. Newer colorimetric tests using colored particles may require fewer steps than colorimetric methods using ELISA.

SENSITIVITY AND SPECIFICITY — On the basis of published reports, no single rapid test has been shown to be clearly superior. Each package insert includes manufacturers' claims of sensitivity (absence of false-negative results) and specificity (absence of false-positives); sensitivity is usually claimed to be 90% to 95% and specificity between 95% and 99%. In clinical use, specificity usually has been higher than 90%, but the reported sensitivity of rapid detection tests has varied between 60% and 95%, depending partly on the culture method used as a control (MA Gerber, *Pediatr Infect Dis J* 1989; 8:820). According to one *Medical Letter* consultant, 60% to 70% sensitivity is typical.

CONCLUSION — Rapid detection tests for group A streptococcal pharyngitis are highly specific but only moderately sensitive; negative tests should be confirmed with a culture.

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Social Security Disability Benefits: An Overview

BRUCE H. ZWECKER, J.D.

ABSTRACT—Disability benefits provided by the Social Security Administration are unique and distinct from other disability benefit programs. Physicians should be cognizant of these distinctions when evaluating a patient who has applied for Social Security benefits. Also, physicians must recognize the limitations of their expertise, as appropriate, when assessing disability.

Introduction

FREQUENTLY, physicians are asked to evaluate a patient's eligibility for Social Security disability benefits. Such requests assume familiarity on the physicians' part with the Social Security Administration's concept of disability and entitlement requirements; unfortunately, all too frequently, such familiarity does not exist. Some physicians acknowledge their lack of expertise and refuse to offer such opinions. Other practitioners confidently proffer opinions which are frequently expressed in inappropriate terms, eg, "temporarily partially disabled," "20% impairment of the lumbar spine." Such opinions effectively demonstrate the authors' lack of familiarity with the many unique factors of entitlement to Social Security disability benefits. Therefore, the purpose of this article is to explain some of the rudimentary concepts of the Social Security disability program.

Two Disability Benefit Programs

1. *Title II Disability Insurance Benefits* (DIB) are available to disabled individuals only if they have worked a requisite number of calendar quarters. The amount of a worker's disability insurance benefit is related to his or her own earnings; that is, the greater the individual's average earnings (and the amount "contributed" to Social Security), the greater the amount of his or her benefit. Since an individual is "insured" based on his or her earnings (hence, the name "disability *insurance* benefits"), his or her income and resources are not relevant. If an individual is found to be entitled to disability insurance benefits, his or her spouse and children are entitled to "auxiliary" benefits. In January1991 the average DIB was $587 per month, while the average disabled worker, spouse, and child(ren) received a combined benefit of $1,022 per month.

2. *Title XVI Supplemental Security Income* (SSI) provides disability benefits to those with minimal income and resources. There is no requirement involving "insurance" (ie, earnings), and an individual who has never worked may be eligible to receive SSI. Because SSI is not related to an individual's own earnings, there are standard federal benefit rates which are established annually. As of January 1991 the standard benefit rate for an eligible individual was $407 monthly, and for an eligible couple (both disabled), $610 monthly. These amounts are thought to represent sufficient income to provide for basic necessities, so any other income received is deducted from these standard rates. Therefore, a disabled individual (without eligible spouse) cannot receive more than $407 per month in other income and still be eligible to receive SSI. DIB is considered income, so an individual who applies for both DIB and SSI and is found disabled might receive only DIB, if the amount of his DIB exceeds the SSI benefit amount. Also, as of 1 January 1991, an eligible individual may own up to $2,000 in resources, while a couple may have resources not exceeding $3,000. Such articles as a home (which is used as the principal place of residence) and one automobile (if necessary for the medical treatment of a specific or regular medical problem) are excluded in determining resources.

Determining Disability

As indicated, disability insurance benefits are provided under Title II of the Social Security Act, while supplemental security income is provided under Title XVI of the Social Security Act. However, the definition of disability for either benefit is the same. Both § 223(d)(1)(A) of Title II and § 1614(a)(3)(A) of Title XVI define "disability" as the "inability to engage in any substantial gainful

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activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months."

All components of the Social Security Administration use the following "sequential evaluation," as set forth in regulations (20 CFR 404.1520 and 416.920), in determining whether an individual is or is not disabled. If an individual can be found "disabled" or "not disabled" after any step, evaluation under subsequent steps is unnecessary.

1. *Is the individual presently engaging in substantial gainful activity*? That is, if he or she is doing "substantial" (significant physical or mental activities, even if part-time) "gainful" (done for pay or profit) work activity, then he or she is not presently disabled. However, the individual may still be entitled to a "closed period of disability" (benefits for a period of disability which lasted at least 12 months but which ended when he or she returned to work).

2. *Does the individual have a severe impairment*? An impairment or a combination of impairments must significantly limit the individual's physical or mental ability to perform "basic work activities." Physically, these include the ability to walk, stand, sit, lift, carry, push, pull, reach, and handle, as well as the capacity to see, hear, and speak. Mentally, basic work activities require the aptitude to understand, carry out, and remember simple instructions, to use judgment, to respond appropriately to supervisors, coworkers and usual work situations, and to deal with changes in a routine work setting. It is especially important for physicians to recognize that Social Security defines a "severe" impairment in terms of functional, not medical, consequences. If an individual does not have a severe impairment, then he or she is not disabled.

3. *Does the individual have an impairment or impairments which "meets" or "equals" an impairment listed in the Listing of Impairments*? The Listing of Impairments describes, for each of the major body systems, impairments which are considered severe enough to prevent the person from doing any gainful activity, without consideration of his or her age, education, and work experience. For an impairment to *meet* a listed impairment, it must be associated with medical findings (symptoms, signs, and laboratory findings) which are *identical* to those listed under the appropriate diagnosed impairment. For an impairment to *equal* a listed impairment, it must be associated with medical findings which are at least *equivalent in severity and duration* to the listed findings. At this step, an individual's functional abilities and vocational factors (age, education, and work experience) are not considered. If an individual suffers from an impairment(s) which meets or equals a listed impairment, then he or she is found to be disabled.

4. *Does the claimant's impairment prevent him or her from doing past relevant work*? In making this determination, the physical and mental demands of the claimant's "past relevant work" (work done for a period of at least three months, within the past 15 years) are compared with his or her "residual functional capacity" (what an individual can still do despite his or her functional limitations). With regard to physical impairments, the abilities to sit, stand, walk, and lift are the most frequently evaluated. In cases involving mental impairments, such factors as the abilities to understand, carry out, and remember instructions and to respond appropriately to supervisors, coworkers, and work pressures are considered in determining residual functional capacity. If an individual retains the residual functional capacity to perform any of his or her past relevant jobs, then the individual is not disabled.

5. *Is the individual prevented from doing other work*? This depends on whether the individual has the residual functional capacity to perform work other than his or her past relevant work, and, considering his or her age, education, and previous work experience, whether he or she can make an adjustment to such other work. This "other work" must "exist in the national economy"; that is, there must be a significant number of jobs, in one or more occupations, existing in the individual's region or in several other regions of the country. Generally, older individuals (over age 50), less-educated individuals (below high school level), and individuals with unskilled work histories or without transferable skills are less capable of adjusting to work other than that which they performed in the past. However, if an individual's functional limitations are such that the "occupational base" (the number of occupations that an individual has the residual functional capacity to perform) is so reduced that there is not a significant number of occupations remaining which he or she is still capable of performing, then that individual can be found disabled, even if he or she is a younger individual, has a high school education or more, and/or has transferable skills from previous work. If an individual with a severe impairment is unable to perform his or her past relevant work and other work, then he or she is disabled.

In summary, an individual can be found disabled in either of two ways: first, on the basis of his or her medical findings alone (the Listing of Impairments), or second, upon consideration of the medical findings, residual functional capacity, and vocational factors (age, education, and previous work experience).

The Administration Review Process

Potentially, there are five levels of review in Social Security claims. In order, they are as follows:

1. *Initial determination*. Generally, an individual files an application for DIB and/or SSI benefits at a district

office. The application and other forms are then forwarded to the Bureau of Disability Determination (State Agency). There, adjudicators develop the file, by requesting medical reports from the claimant's treating sources and, if necessary, sending him or her, at government expense, for "consultative examinations" to physicians under contract. The State Agency, which has a medical review staff, makes an initial determination" whether the individual is or is not disabled and notifies the individual.

2. *Reconsideration.* If a claimant wishes to appeal an initial determination, he or she may file a "request for reconsideration" at the district office within 60 days after receiving the notice of initial determination. State Agency staff who were not involved in the initial determination review and develop the file and make a "reconsidered determination."

3. *Hearing.* If a claimant is dissatisfied with the reconsideration, he or she may request a hearing before an Administrative Law Judge (ALJ) from the Office of Hearings and Appeals (OHA) within 60 days after receiving the notice of reconsideration. If desired by the individual, the ALJ will render a "decision" based only on the evidence of record. However, generally, the individual appears personally at a scheduled hearing where, for the first time, he or she is permitted to review the evidence in the file and orally present his or her case. Also, he or she has the right to be represented by either an attorney or layperson. The ALJ can arrange for consultative examinations, subpoena witnesses, and seek assistance from physicians ("medical experts") and vocational counselors ("vocational experts") under contract with the Social Security Administration. He or she then issues a decision.

4. *Appeals Council.* If the individual is dissatisfied with the decision of the Administrative Law Judge, he or she may request, within 60 days of receipt of the ALJ's decision, that the Appeals Council review the decision. The Appeals Council is located in Falls Church, Virginia, and does not hold hearings. Instead, the claimant may submit documentation or written argument. Generally, when the Appeals Council agrees with the ALJ's unfavorable decision, it merely denies the claimant's request for review, rather than issuing a new decision. If so, the ALJ's decision becomes the final action of the Secretary of Health and Human Services. The Appeals Council can also grant the request for review and either remand the case to the ALJ for re-hearing or simply reverse the ALJ's decision.

5. *Federal Court Review.* If the individual is dissatisfied with the action of the Appeals Council, he or she may, within 60 days of the date of receipt of the Appeals Council's action, file an appeal in federal district court. If the individual or the Social Security Administration is dissatisfied with the decision of the district court, either may appeal to the court of appeals and, ultimately, to the United States Supreme Court.

Conclusion

In summary, some observations, apparent and not so apparent, are in order. An individual is not entitled to Social Security disability benefits merely because he or she is unable to perform his or her usual occupation. Social Security disability criteria require the individual to be unable to perform *all* past relevant work; he or she must also be unable to perform any other work which exists in the national economy. Further, it cannot be overemphasized that, by regulation, a finding of "disabled" under the Social Security Act cannot take into consideration whether work exists in the claimant's immediate area; whether a specific job vacancy exists for the individual; whether the individual would be hired if he or she applied for work; employers' hiring practices; cyclical economic conditions; and whether an individual wishes to do a particular type of work.

By contrast, workers' compensation programs (under individual state law, as opposed to the federal Social Security program) provide compensation for both "total incapacity" and "partial incapacity." Additionally, such programs typically take into consideration "marketability," ie, whether other work is "available" in the same locality, as well as whether the individual is able to secure work. Also, certain impairments have a "scheduled" length of incapacity. By contrast, Social Security disability is not established for a finite number of weeks. The "duration requirement" involves an impairment(s) expected to be fatal or which has already lasted or can be expected to last at least one year. Although technically the duration requirement refers to the impairment(s), the prevalent position is that the disability (ie, the inability to engage in substantial gainful activity) must also satisfy this criterion. Typically, unless he or she has returned to work or there has been significant medical improvement, an individual found to be disabled at a certain date is found to be continuously disabled through the indefinite future.

Finally, it should be clear that "disability" under the Social Security Act ultimately is a legal concept which is premised on both medical and vocational factors. For this reason, physicians should be loathe to render unequivocal conclusions about "disability," as opposed to purely medical concerns.

In this same view, the American Medical Association has stated:

> It is particularly important to understand the distinction between a patient's **medical impairment,** which is an alteration of health status assessed by medical means, and the patient's **disability,** which is an alteration of the patient's capacity to meet personal, social, or occupational demands, or to meet statutory or regulatory requirements, which is as-

sessed by nonmedical means. In a particular case, the existence of permanent medical impairment does not automatically support the presumption that there is disability as well. Rather, disability results when medical impairment leads to the individual's inability to meet demands that pertain to nonmedical fields and activities....

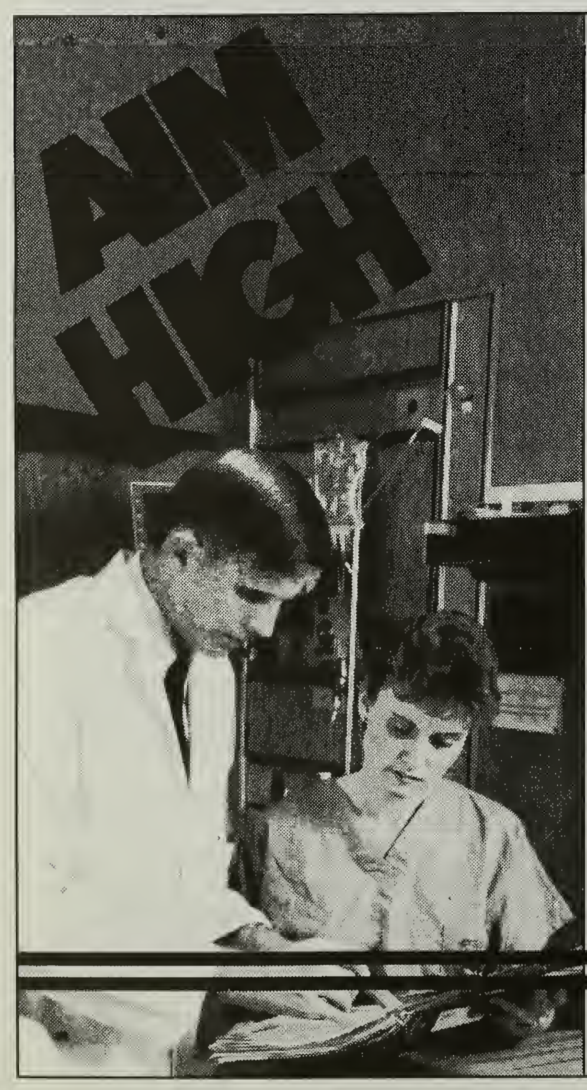
The physician who makes a determination about impairment must keep in mind that a permanent impairment rating is not the same as a disability rating. Permanent medical impairment is related directly to the health status of the individual, whereas disability can be determined only within the context of the personal, social, or occupational demands, or statutory or regulatory requirements that the individual is unable to meet as a result of the impairment...

In general, it is not possible for a physician, using medical information alone, to make reliable predictions about the ability of an individual to perform tasks or to meet functional demands.[1]

Consequently, when asked for their opinions about patients applying for Social Security disability benefits, physicians should consider the limitations of their medical expertise in framing their responses. Accordingly, they may prefer to state only what impairments are established by objective medical signs and laboratory findings. Also, but only if the physician feels sufficiently competent to render an opinion, he or she may wish to estimate what functional restrictions, in his or her opinion, can reasonably be anticipated. By providing such information, the physician fulfills a vital, effective function in the disability determination process, without usurping or being forced to assume the role of ultimately deciding who is and who is not disabled. Such decisions, with appropriate medical and vocational input, should be left to the Social Security Administration.

REFERENCE

1. Guides to the Evaluation of Permanent Impairment, American Medical Association, 2nd ed., 1984: vii-x.



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AIR FORCE

Final Medicare Anti-Fraud and Abuse Safe Harbor Regulations

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AFTER an almost two-year delay, the final Medicare Anti-Fraud and Abuse Safe Harbor Regulations were issued by the Department of Health and Human Services on 29 July 1991. As expected, they significantly limit the ability of physicians and hospitals who are Medicare or Medicaid providers to enter into certain types of relationships. Although their stated purpose is to reduce fraud and abuse in the Medicare and Medicaid programs by ferreting out improper referral practices, the regulations are quite stringent and may affect legitimate business arrangements, as well.

The regulations establish "*safe harbors*" for some types of business arrangements. If the arrangement fits within a safe harbor and meets all of its requirements, it is protected from prosecution. If it does not, it has no safe harbor protection but is not automatically presumed unlawful.

If the arrangement is found to be abusive, violators may face severe penalties including the possibility of a prison sentence of up to five years, fines of up to $25,000, and permanent exclusion from the Medicare and Medicaid programs.

The regulations are immediately effective and do not allow any "*grace period*" for coming into compliance. A number of joint ventures established by physicians and hospitals in the past may have to be restructured or sold in order to fit within a safe harbor. Health care providers involved in business ventures not protected by a safe harbor should carefully evaluate the risks associated with remaining in the venture.

This memorandum discusses the safe harbors available under the regulations, including those applicable to investment interests, space and equipment rentals, sales of practices, referral services, personal services and management contracts, employment relationships, warranties, discounts and group purchasing, and waivers of beneficiary coinsurance and deductible amounts.

Investment Interests

All business arrangements involving investments by physicians in services or entities to which a referral could be made should be reviewed in light of the investment interest safe harbor. An unofficial "*leaked*" version of the safe harbor regulations would have required that no more than fifty percent of the owners of a health care joint venture or limited partnership be in a position to make or influence referrals. The final safe harbor regulations restrict the investment criteria even further. Now,

- *no more than forty percent of the ownership interests* may belong to individuals or entities in a position to refer patients to the venture;
- *no more than forty percent of the gross revenues* of the business during the prior fiscal year or the previous twelve months may be derived from investor referrals;
- ownership shares must be marketed *without regard to the purchaser's potential to refer patients* to or otherwise generate business for the venture;
- *continued ownership may not be conditioned on referrals;*
- the entity *may not loan funds to or guarantee a loan for an investor who is in a position to make or influence referrals* to or otherwise generate business for the entity; and
- the amount of payment to an investor in *return for his investment interest must be directly proportional to the amount of capital investment* of that investor.

This article is a summary of regulations appearing in the *Federal Register*, 29 July 1991, Vol. 56, 35952-87.

The authors are members of the law firm of Wiggin & Dana, Councellors at Law, New Haven.

Any investor who does business with the joint venture, including both physicians and hospitals, is considered to be a referral source and is subject to the 40 percent cap.

An investor can be either an *individual* or an *entity* such as a hospital, and the investment interest may be held either *directly* or *indirectly.* Thus, if a family member of a referring physician holds an investment in a joint venture to which the doctor is in a position to refer patients, the physician will be viewed as having the ownership interest. Similarly, if a hospital creates a holding company or a sister corporation to hold investment interests in a joint venture to which the hospital may refer patients, the ownership interests will be attributed to the hospital.

A safe harbor also was created for investments in large publicly traded entities which, within the previous fiscal year or previous twelve-month period, possess more than $50,000,000 in undepreciated net tangible assets.

Space and Equipment Rental

A safe harbor has been established for certain space and equipment rental arrangements among health care providers who are in a position to refer patients to each other. The safe harbor is intended to discourage special rental arrangements that may be a direct or indirect financial inducement to refer patients for unnecessary services. In order to qualify for the safe harbor, rental agreements for space or equipment must be for *at least one year*, in writing, and must specify the premises or equipment covered. Rental charges for space or equipment

- must be *set in advance*;
- must be *consistent with fair market value* in arm's-length transactions; and
- *must not be determined in a manner that takes into account the volume or value or any referrals* or business otherwise generated between the parties for which payment may be made in whole or in part under Medicare or Medicaid.

Premiums charged for rental of space on account of the proximity of the leased premises to a referral source will cause a lease to *fall outside the safe harbor. Rent discounts offered to physicians* who are in a position to refer patients also *are not protected.* However, certain rent concession arrangements offered by hospitals to staff physicians may be protected under a separate physician recruitment safe harbor which has not yet been issued.

"Per procedure" equipment leases that vary rent payments based on the number of procedures performed are *not protected.* Similarly, a "wear and tear" clause that varies rent in order to account for maintenance costs and the useful life of the equipment will cause the lease to fall outside the safe harbor. The enforcement arm of the Health Care Financing Administration has acknowledged that there might be legitimate business reasons to include such a provision in a lease, but it declined to provide safe harbor protection and will examine such provisions on a case-by-case basis as the need arises.

Sale of Practice

In order to fall within the safe harbor established for the sale of a practice by a practitioner,

- the *sale must be completed within one year* from the date of the first agreement pertaining to the sale; and
- the *selling practitioner must not be in a professional position to refer patients* to, or otherwise generate business for, the purchasing practitioner *after one year from the date of the first agreement* pertaining to the sale.

Practices that are sold as a result of a physician's retirement or some other event that removes the physician from the practice of medicine or from the service area in which he was practicing are protected by the safe harbor. On the other hand, if a physician sells his practice to a hospital and the physician continues to practice on the hospital's staff, the sale will *not* receive safe harbor protection.

Referral Services

Medical associations or hospitals may operate services that refer physicians or other health care providers to the public. In order to receive safe harbor protection, a referral service must meet certain requirements that include the following:

- the service *may not exclude* any doctor or health care entity that meets the qualifications for participation in the service;
- any payment made by a doctor or health care entity to participate in the referral service *must be assessed equally against, and collected from, all participants*; and
- such payments *may not be based in any way on business generated* by the doctor or health care entity for the referral service.

In addition, the referral service also must make the following disclosures to the patient:

- the manner in which it selects the doctors and health care entities that can participate in the service;
- whether the doctor or entity has paid a fee to the referral service;
- the manner in which it selects a doctor or health care entity for the patient;
- the nature of the relationship between the referral service and the group of doctors and health care entities to whom it could make the referral; and

- the nature of any restrictions that would exclude a doctor or entity from continuing as a participant in the referral service.

Personal Services and Management Contracts; Bona Fide Employees

Many health care entities enter into contractual arrangements with other providers to provide services such as peer review, medical or surgical consulting, or administrative activities. To receive safe harbor protection, such agreements must be in *writing, for at least one year*, and *specify the services to be provided by the agent*. In addition, the aggregate compensation paid to the agent

- must be *set in advance*;
- must be *consistent with fair market value* in arms-length transactions; and
- *must not take into account the volume or value of any* referrals or business otherwise generated between the parties for which payment may be made by Medicare or Medicaid.

Services that can be performed in one year still can qualify for safe harbor protection. The one-year period "restricts the period within which the contract terms may not be changed, and not the time within which services under the contract may be performed."

Payments made to bona fide employees are protected by a safe harbor.

Warranties

In order to qualify for safe harbor protection for warranties offered to purchasers by a manufacturer or supplier of an item,

- the buyer must report any price reduction of an item, including a free item, which was obtained as part of the warranty when filing cost reports or claims for payment, and must supply certain other information to the Medicare or Medicaid agencies upon request; and
- the manufacturer or supplier must report the price reduction of the item (including a free item) which was obtained as part of the warranty, on the invoice or statement submitted to the buyer, and inform the buyer of its obligations to provide the information specified above.

Discounts and Group Purchasing Organizations

Certain discounts offered by a seller for goods or services qualify for safe harbor protection. These include *reductions in price for goods or services based on an arm's-length transaction*, as well as *rebate checks, redeemable coupons, and credits subject to specific conditions*.

However, many common discounts are not protected, including

- cash payments,
- furnishing goods or services without charge or at a reduced charge *in exchange for an agreement* to buy another good or service ("bundled purchases"),
- price reductions applicable to certain payers but not to Medicare or Medicaid, or
- routine reduction or waiver of a beneficiary's coinsurance or deductible.

Thus, if a vendor of durable medical equipment gives a physician a free piece of equipment (e.g., a personal computer) in exchange for the physician's promise to buy a certain quantity, the discount does not qualify for safe harbor protection.

For buyers required to file Medicare cost reports, discounts

- must be earned based on purchases within a single fiscal year,
- must be claimed in that year or the next fiscal year,
- must be fully and accurately reported in the buyer's cost report, and
- must be reported with specified information from the seller if requested by the Department of Health and Human Services or a state agency.

In addition, the seller must inform the buyer of the buyer's obligation to report the discount. The seller also must either report the discount on the invoice or, if the value of the discount is not known, report the existence of a discount program and report the discount when its value is determined.

A safe harbor was created for payments from vendors to entities authorized to act as a group purchasing organization for Medicare or Medicaid providers. The agreement between the organization and the vendor must be in *writing* and must *specify the amount the vendor will pay the organization*.

Waiver of Beneficiary Coinsurance and Deductible Amounts

In order to qualify for the safe harbor created for waiver of beneficiary coinsurance and deductible amounts

- if the amounts are owed to a hospital for inpatient hospital services for which Medicare pays under the prospective payment system, *the hospital must not later shift the burden of the reduction or waiver onto Medicare, Medicaid, other payers, or individuals* (such as by claiming it as a bad debt);
- *the hospital must offer the waiver or reduction with-*

out regard to the reason for admission, the length of stay of the beneficiary, or the diagnostic related group for which the claim for Medicare reimbursement is filed; and

- the hospital's offer to reduce or waive the coinsurance or deductible *must not be made as part of a price reduction agreement between a hospital and a third-party payor.*

Conclusion

Physicians should examine *all* of their health care investments and joint ventures for compliance with these regulations. The following are some warning signs of noncompliance:

- physician and/or hospital investors are in a position to refer patients or generate business for the venture;
- rental payments for office space or equipment are inconsistent with fair market value;
- rent for equipment is on a "per procedure" basis;
- an investor's return is disproportionately large compared to his initial capital investment or varies with the amount of referrals made or procedures performed;
- a venture circulates information on the referral patterns of its investors;
- a venture explicitly or implicitly encourages investors to refer patients to it;
- a vendor offers discounts to providers in exchange for an agreement to purchase a certain quantity of goods or services.

Many existing physician investments and joint ventures were structured in a manner which fails to comply with safe harbor requirements and therefore places the investing and referring physicians at some risk. Physicians should consult their legal counsel for advice concerning compliance with the safe harbor regulations.

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Squirt

E. TREMAIN BRADLEY, M.D.

WATER we tend to take for granted unless there is a drought— or a flood. Its potential is tremendous. Never underestimate the power of water: from towering falls to the few drops that relieve a parched mouth. Without water, vegetation withers and dies. So do people. With it, things grow and thrive. So do people.

A glass of tap water first thing in the morning gets the body functioning. The bladder gradually fills and must be emptied. That is the moment for another glass of water to be gulped (sipping usually diminishes the quantity consumed). Thus the kidneys keep flushed, healthy, and effective. Various circumstances, of course, may require modification of all this.

Ocean waves can wash away beaches. Some good warm water can do wonders to a sore throat. Just fill an enema or douche bag with very warm water (adding salt may help) and hang it high near a sink or tub. Pinch off the hose with one hand and with the other aim the straight nozzle (or just the end of the hose) straight up, like a fountain. Take a deep breath through the mouth and hold it, leaving the tongue down and out of the way. Then lean over and let the water squirt up through the mouth toward the posterior pharynx. It will tend to gag at first, so pinch it off and come up for air. After several attempts at this, the warm water will be tolerated by the pharynx and will 1) rinse off bacteria, phlegm, mucus, purulent secretions and 2) poultice the area, the heat stimulating circulation and promoting resistance and healing.

Long unsung is a water jet device: the Water Pik. Dentists complained that this intermittent jet forced bacteria deep into the pockets under the gum, causing damage and infection. Maybe so, but doubtful! To use the instrument properly, direct the stream at right angles to the long axis of the tooth, to where it meets the gum. The setting should be low at first, gradually increasing to the highest as the sensitivity of the gums diminishes. The jet should also be directed between the teeth. I have done this after thorough brushing at night for over 20 years, with essentially no tartar and no cavities. When my wife was advised to have gum surgery for gingivitis and deep pockets, we declined and put her on a regimen of brushing, flossing, and water piking. Within a year her gums returned to normal health. For two years now as an experiment she discontinued the flossing. Her gums remain healthy and no cavities have appeared. As reported in *Dentistry Today* Vol. 10, No. 7, Surindar N. Bhaskar, D.D.S., a periodontist in Monterey, California, strongly recommends the use of a water jet device as the most important home care dental tool.

Further evidence. In Florida they lay sheets of plastic under the sand to keep the weeds down. Since it kept the water out too and I wanted things to grow, I pushed back the sand and tugged and tore out the plastic. Result: every fingernail was loosened from the nail bed and sand had been driven deep under the nails into the blood that had collected. I foresaw infection in these subungual hematomata. What to do? It wasn't fun, believe me! But I took the Water Pik and squirted under each nail—a little at a time—until the sand and clot were gone. No infection ensued and the nails eventually grew back well attached. This convinced me of the fallacy about driving bacteria under the gums.

I just discovered that at the Winsted Memorial Hospital a Water Pik is used for cleaning out the wax from ears. First, a little Debrox or peroxide is dropped into the canal in order to loosen up the contents. After five or 10 minutes the ear lobe is pulled upward and back to straighten the canal and the Water Pik tip is placed just inside. The lowest setting should be used. The tip can be rotated some as the water squirts in. What comes out can be caught in a kidney basin or a towel held against the neck, or can be allowed to fall away freely. Better than the syringe method.

E. Tremain Bradley, M.D., solo practice of General Surgery, retired to Norfolk, Conn.

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Editorial

Guest Editorial

Speaking Up for Education, Standing Up for the Profession

I am taking this opportunity to offer some thoughts about the 1991 Annual meeting of the AMA Hospital Medical Staff Section, which had to its credit the greatest number of newly certified HMSS Representatives recorded since the first year of the Assembly.

Perhaps because there were so many new HMSS Reps, there were a noticeable number of fresh sentiments being expressed, questioning eyes and timid sorts of comments behind the scenes. Among them were statements such as, "We've got to do something," and "I really didn't feel I knew enough to get up and talk, but if I had, I don't think you could have shut me up."

The effort in this commentary will be to build an argument, based on comments such as those. It is a commentary on the type of education that physicians regrettably need to survive in the current "hassle" climate. It will take a few paragraphs to get there. I ask for your patience.

I had the honor and the pleasure of visiting with a number of these new HMSS Reps, whose eyes danced and whose minds were fired by the depth and breadth of the information they were getting from the HMSS Assembly meeting—from the reference committee hearings, the education programs, the formal caucuses and the informal conversations. Each of these physicians sensed that they had learned so much. They were also stymied, to some extent, by all that they don't know.

Now that is sad.

These are men and women who have probably been among the best students in every class they ever attended. They are probably people who are more informed than most of the people they talk to every day. They are individuals who probably know the anatomy inside and out, but they may also be people who are adept in art, historical commentary, construction, aviation and auto mechanics.

These are the same people who are intimidated and made to feel dumb about the world in which they live and work. That's because they practice medicine. They are doctors. They didn't study regulation in school, they may not have studied government. In all likelihood, they didn't study reimbursement issues or the way other nations run their health care systems.

Yet in the decade of the '90s these physicians have to know all that—just so they can feel effective discussing medical staff bylaws, joint ventures or other self-governance issues with their hospital administrator, just so they can present a strong case to a PRO reviewer, just so they can defend themselves on the phone with managed care companies. Just so they can survive.

Again, that is so sad.

But it is also challenging for all of us—those who practice medicine, and those who wish to support those who practice medicine.

In analyzing it, it appears that a decade or more of continuous, escalating attacks and encroachments on clinical autonomy and professional integrity have had the effect of making very bright people feel like they don't know enough to stand up for themselves, their education, their expertise, their profession.

In defense of themselves, they've gotten angry and emotional about being intimidated and professionally emasculated. But somehow, at this meeting of grassroots physicians, it seemed clear that they now believe they have to learn new skills to be able to stand up for themselves on the front lines of patient care. They need education in reimbursement, in medical staff legal affairs, in public relations and negotiations. And they need that knowledge just to survive—just to practice medicine.

So what we have to do in organized medicine, as the support system for practicing physicians, is provide that education. We need to provide it where they live, where they work. We need to provide it in ways that are physician-friendly, not association friendly. We need to help.

This is my second point: We will try.

We, the AMA, will try to package programs, working with state and county medical societies, to get the information and education out to you. We will try to help you develop the skills you need.

It occurred to me, however, in the early morning hours following the HMSS Annual Meeting, that there is another avenue.

At the annual and interim meetings of the HMSS Assembly, and at the AMA House of Delegates meetings that follow, there is some of the best education available to medical staff representatives. It is in this forum of enormous involvement and intense commitment to the practice of medicine that medical staff issues are debated, that education programs about national issues and gov-

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ernment affairs are presented. It is at these meetings that extensive information is derived from state caucuses and informal networks among professional peers.

If HMSS Representatives can attend just one meeting each year, between the education derived from the meeting and the programs offered at the House of Delegates meetings, they will return to their medical staffs significantly more skilled in the areas they really never wanted to know about, but absolutely need to learn about in order to effectively survive.

And if you can't attend a meeting, if you can't take four days away from your practice, as a certified HMSS Representative, you can receive the information in the mail. You can find a physician friend who can be an Alternate Representative who might attend the meeting for you. And you can ask for help by phone and become a part of a vast AMA network of information.

It occurred to me, too, that HMSS Reps can make a difference by meeting once a quarter with their county medical societies to discuss medical staff issues. They can attend a state HMSS meeting once a year and urge the state medical society to provide an educational program that focuses on a useful medical staff issue. And when you need to, call on the AMA to offer a program to your medical staff. It can be done.

Physician education is a serious issue. And the new HMSS Reps, more than any of the seasoned participants, brought home the battle cry that the education that is needed goes beyond medical education.

But one thing, physicians, that you do need to know more than anything else, is that you do know enough to speak up for your beliefs. You do know your profession. You do know what regulation, unfair reimbursement, and other second guessing of clinicians is doing to the patients in your offices, and to your sense of professionalism. You do know how to make a change. So don't be afraid to stand up. Because you do know what you're talking about.

Barbara Dolan

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SAVE THE DATES

50 Years Ago

From *The Connecticut State Medical Journal*

December 1941

EDITORIALS

The Medical Student in the Draft

Considerable editorial comment has appeared reprimanding the medical student for not showing more patriotism by applying for a commission in the Army. He has been termed a slacker and a draft dodger and calumny in plenty has been heaped upon his head. True, he is in danger of being drafted but still he does not enlist. In common with the group of physicians but recently entered upon their life work he is defended by the Editor of the *Journal of the South Carolina Medical Association*.* The Southern editor believes that this group of young men do not feel that the Army needs them just now. He expresses the opinion that they themselves do not believe young physicians need the same amount of training for military service as do the draftees and that by remaining at home they are serving the public in their present location.

At the Secretaries Conference in Chicago (see page 915) it was made very clear that the arrangement whereby medical students are at present exempted from the Selective Service Act is by a gentleman's agreement only and may be terminated at the will of either or both the Surgeon General of the Army and the Surgeon General of the Navy. The medical student during his first two years, if scholastically satisfactory, is allowed to continue his studies. During his last two years and during the first year of internship he is expected to enlist in the Medical Administrative Corps as a Second Lieutenant and as such will not be drafted. At the end of one of internship he is obligated, by virtue of the fact that he has been immune to the draft, to apply for a commission in the Medical Corps, U.S. Army or U.S. Navy. He may not be acceptable but the obligation to apply for a commission nevertheless remains.

The results have not fulfilled the expectations. We find that many third and fourth year medical students and first year interns still waiting in the hope that they will not be expected to do anything but what they may have originally planned. The fault does not rest entirely with the student. In many medical schools information has not reached the student advising him as to his proper course. The faculty and administration of some medical schools have not been too cooperative. Doctor Abell, Chairman of the Committee on Medical Preparedness of the A.M.A., warns us that if medical students do not show their patriotism the Selective Service Act still holds and exemption, not being written in the law, may at any time be rescinded.

There should be no question of a prompt and wise decision by every medical student, at least in Connecticut, once he is properly informed.

Peptic Ulcer Today

The medical and surgical treatment of peptic ulcer continues to undergo periodic changes. Back of these repeated changes is probably our lack of knowledge of the specific cause of the disease.

Many men can recall the use of silver salts in this condition, the premise being to stimulate healing of the ulcer. This has long been discarded. All know of the use of sodium bicarbonate alone, in an attempt to neutralize the acidity. The chemistry of this is now known to swing over to the acid side. Some are familiar with the use of foreign proteins and emetine and histidine preparations. In general these are not accepted. The council recently accepted aluminum hydroxide, the preparation commonly called amphojel. In accepting it, the council has insisted upon the name aluminum hydroxide gel. The so called Sippy regime has had and continues to have the largest following. This regime or one of its many modifications is probably the accepted method of managing the disease.

The surgical approach has gone through similar changes. Pyloroplasty, gastroenterostomy, excision of the ulcer have all had their proponents. At present the surgical procedure of choice seems to be subtotal gastrectomy. On physiological and pathological standards this procedure seems sound.

In an article in this issue of the journal, Sara M. Jordan outlines the problems confronting one in the diagnosis and proper management of the condition. She pays particular attention to the danger of superimposed malignancy in recurring ulcers, the possibility of mistaking early malignancy for ulcer and the difficulties associated with the diagnosis of ulcer on the posterior wall. Doctor Jordan's advice, as one would expect from her wide experience, is excellent.

At the present time, there are some men who doubt that this condition can be cured medically or surgically. Fortunately these are in the minority. It may be safely said that the last word on peptic ulcer has not been uttered. This is as it should be. Medicine will not be satisfied until a cure is established. Until then medicine will keep changing in its endeavor to control this disease even though these changes be called revolutionary.

—Editorials from *The Connecticut State Medical Journal*, December 1941.

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S.K. Nallainathan, 377-5988

Pediatric Neurosurgery:
Kenneth I. Lipow, 384-3805

The Brokers

The brokers, quite simply, are the robber barons of the American health care system. They collect all the monies, take their costs and profits, and use the balance to pay the physicians and the providers for services rendered to the users of the great American medical system.

The government, with its large Medicare program, is the leading broker. HCFA admits only to incurring administrative costs of 1.4% for Medicare A and 3.7% of Medicare B payouts, roughly 2% on average. According to the AMA, this may reflect the costs of governmental administration, but cannot and does not reflect the administrative costs of the insurance companies retained as fiscal intermediaries which actually pay the bills and administer the many regulations imposed on hospitals, providers, and physicians alike. Administrative costs of 8% to 11% would not be unusual in the private health insurance industry, even without a profit factor. To these numbers must be added the cost borne by the physicians for administering the paperwork for their side of the Medicare and other programs. According to the American Society of Internal Medicine, the average visit generates *ten* pieces of paper. In addition, the hospitals attribute as much as 37 cents of every dollar they spend to paperwork done on behalf of the government and the other brokers.

- *Government & insurer administration:* 12% to 15% of the health care dollar
- *Physician's administration:* 20% of the 20% received: 4%
- *Hospital administration:* 37% of the 60% received: 22%
- *Total administrative cost of Medicare:* 38% to 41%

Not even counted are the additional administrative costs connected with the myriad of private supplementary policies sold to cover the 20% of "allowable" charges NOT paid by Medicare. Besides administration, these policies also have heavy acquisition costs involving marketing as well as commissions.

Thus, the scheme set up by the government is costing 38% to 41%+ to administer. No wonder there is not enough to pay the physicians and the providers, and to allow the utilizers full and prompt treatment. It is interesting that the federal administration has recently set up a committee to investigate the 10%-18% waste on the administrative side of Medicare. The other trick the government plays is to delay payments for three to six months. One must remember that at 6% per year, a million dollars grows by $5,000 every month. This amounts to billions in the course of a year. It is possible to argue that the government provides many people with jobs and that these employees all pay taxes. But, when their work is inefficient and unnecessary, there is tremendous financial waste. It is also true that when Congress and the general public look at the total expenditure for health care, the assumption is that all of the money goes directly to provide health care for the American people. It does not. Some 40%, siphoned off for administration, buys no care and cures no ills.

The private insurance companies, HMOs, and PPOs make no bones about the fact that health insurance is a business, and that they are in it to make money. They even build in a profit line of at least 5%, not including the interest income developed by delaying payments to the physicians and the providers. This can be quite considerable. Private insurance companies generally do not have the tremendous waste factor that is built into government systems.

To increase their profit margins and to make them look good, the brokers early on realized that they had to control both the physicians and the other providers. They started by controlling the length of stay by utilizing DRGs. For the most part, the brokers were outmaneuvered by the hospitals, which simply added extra diagnoses. These brokers then turned to the physicians, which is where we are today. With the RBRVS, they put physician charges on the table and showed the enormous differences between the procedural and the cognitive physicians. Using this as a wedge, they have divided the physicians into groups. The brokers, by controlling certain groups of physicians, will eventually control the divided house of medicine. Then they, not the physicians, will become the drivers of the American health care system.

The government, through Medicare, has been the "loss leader," and even today, in 1991, it pays physicians 1984 fees. Medicaid pays even less. There is nothing the physicians can do about it. The insurance industry, aided and abetted by big business, which has had to bear the brunt of medical care costs, has followed Medicare's example. Interestingly, the hospitals have tried to unite against the brokers by creating the Voluntary Hospital Association (VHA). However, the VHA only allowed a select group to join and excluded the others, so the hospitals, too, at this point in time, are a divided group. It must be obvious that with three quarters of a trillion dollars at stake, only the strong will succeed.

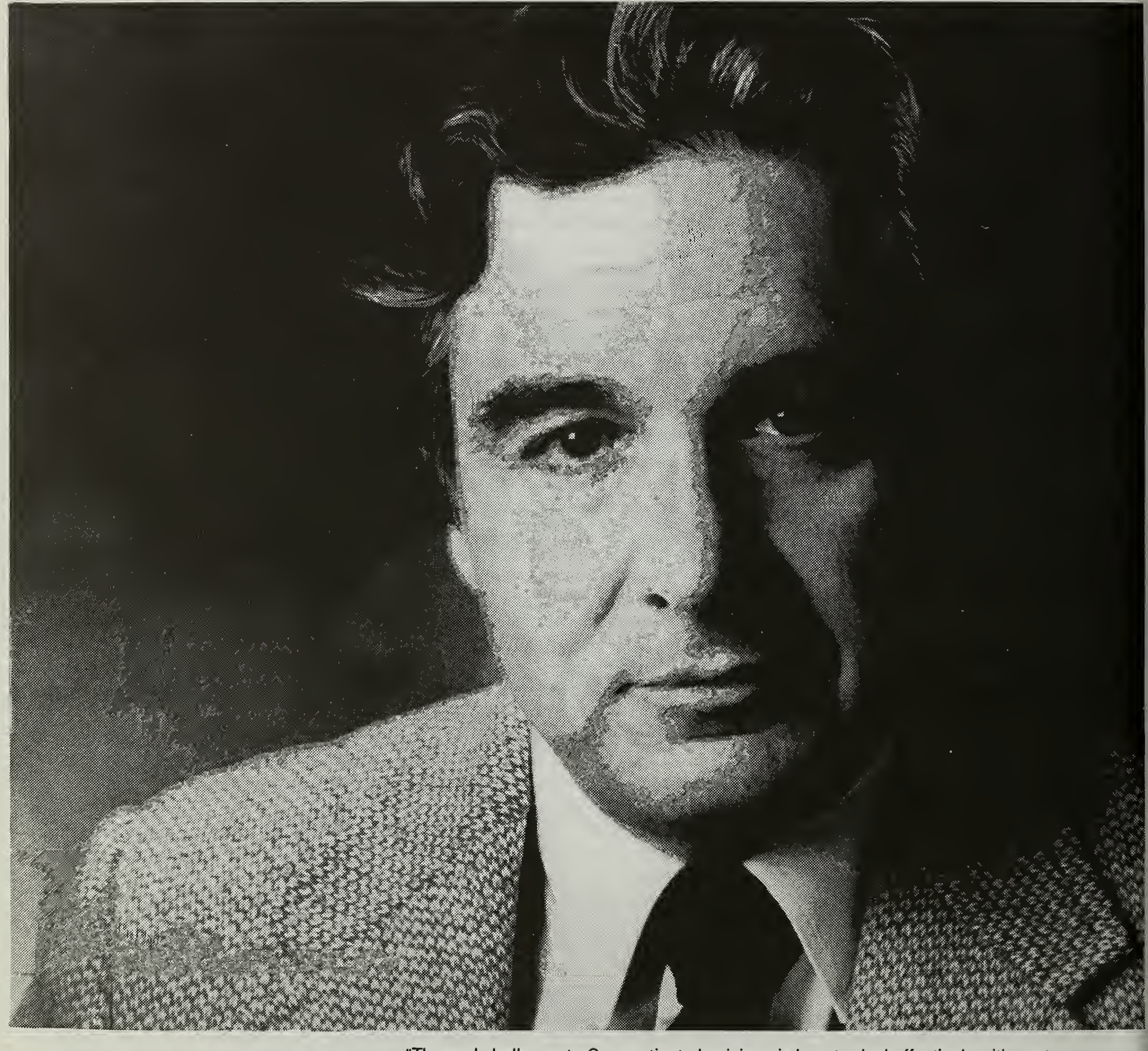
I have kept the word "rationing" till the end, because this is the other way that the brokers can control costs. If they only allow 50% of the cataracts discovered in one week to be removed then the other half has to be done the second week. All those discovered in the second week will be done in the third and fourth weeks. This is how a waiting list is built, and rationing becomes part of the system. So, by waiting a few months or years for new eyes or hips, the rationing concept would become reinforced, as it has in Great Britain. But I am afraid that the American public are less docile. They would rather sue than queue.

The question really is, "Are the American people willing to pay for the best medical system in the world?" And if so, are they willing to sit back and allow the brokers to walk away with all the profits?

A lot of what I have written in the last three months has been basic and preliminary. Next month I will examine how the players—namely, the physicians, the providers, the utilizers, and the brokers—mix and interact, and what can be done to produce a successful system that will be acceptable to all.

Anthony P. Redmond, M.D.
President

"I'm accountable to my patients, not to an insurance company. That's just the way I operate."
—Dr. Vincent Catrini, General Surgery, Middletown, CT



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REFLECTIONS ON MEDICINE

Mortality and Disease

ROBERT U. MASSEY, M.D.

OVER 10 years ago an elderly physician friend remarked that the sexual revolution had resulted from birth control pills and penicillin. "Why don't you people who are interested in medical history write about that?"he asked. "Hardly a new idea," I remarked, "and anyway it's not that simple." That conversation came to mind after reading Ellen Goodman's column last month (Hartford *Courant,* 22 November 1991) in which she reflected on our moralizing and medicalizing attitudes post-Magic Johnson. Among other things she wrote, "Premarital sex is here to stay."

Among the truths we may learn from history is that not much is here to stay. Another apparent truth about social behavior is that trends and fashions are set by the upper classes, the rich, famous, and powerful; they then trickle down through the layers of the middle classes finally to be taken up by the lower classes and the underclass, by which time they have been mostly rejected by those who originated them. Follow the popularity of cigarettes, hard liquor, and cocaine during the last 100 years and this trickle-down pattern seems to hold. Premarital sex, promiscuity with its accompanying sexually transmitted diseases, and drug abuse, although hardly absent from the upper classes, are now devastating problems for the lower classes. We are reminded over and over that no one is immune, all are at risk, but that is only partially true; the prevalence of these symptoms of social disorganization increases dramatically as we move downward through the social classes. What we have to fear most is trend-setting misbehavior in high places!

The medical historian Oswei Temkin traced this behavioral pattern through its twists and turns in his essay, "On the History of Morality and Syphilis."[1] Until syphilis was *generally* recognized as a venereal disease, perhaps about 1520, the new pestilence was considered to result from general godlessness, especially in foreigners, but not necessarily individual impurity. A few years later the "mal venerien" was clearly seen as chastisement for sexual impurity. Among the nobility, however, it was the cavalier's disease. "Erasmus of Rotterdam," wrote Temkin, "tells us that a nobleman who had not contracted the disease was considered 'ignoble and rustic.'" The lower classes, on the other hand, were chastised for their immorality; soldiers, an in-between group, by the very nature of their occupation, were expected to contract the French pox but among the nobility syphilis was the badge of amorous conquest. This attitude reached its climax in the mid to late 18th century, immortalized in such works as Casanova's memoirs and Mozart's "Don Giovanni."

Quite suddenly, especially after the French and American revolutions, there appeared a change in direction toward the bourgeois values of frugality and family fidelity. Especially in English and German literature the new morality was extolled, and the ideal life became one of simple virtue and piety. Contrast the idealism of premarital purity, marital faithfulness, and the sanctity of the family in the novels of Jane Austen with the exploits recounted in Henry Fielding's *Tom Jones* or the memoirs of Casanova only a few decades earlier. The Victorian upper classes during the century that followed were hardly models of purity, but they mostly kept quiet and pretended to the more puritan ideals of the rising middle classes. What was interesting, Temkin noted, was the rapidly declining incidence of syphilis among students, "once Storm and Stress and the French Revolution have roared past, …."

Recurring cycles of license and puritanism may be traced throughout our history, as well as throughout the histories of other cultures. Magic Johnson's, and the Kennedys', habits of profligate living may indeed soon become outmoded; in fact, the sexual revolution, which was no revolution anyway, may be about to turn back into history. Even Magic, it has been said, has recently been soft-peddling his safe-sex message in favor of no pre- or extramarital sex.

REFERENCE

1. Temkin O: On the history of "morality and syphilis," in *The Double Face of Janus and Other Essays in the History of Medicine,"* Baltimore, Johns Hopkins University Press, 1977, pp. 472-84.

ROBERT U. MASSEY, M.D., Professor, Division of Humanistic Studies, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington.

Access to Food Constitutes a Human Right

World hunger is an ever-present scourge that claims 35,000 lives each day. We so frequently take for granted our job opportunities, our very comfortable homes and our ability to feed, clothe and educate our children. While we take for granted all this abundant goodness, three children are dying of starvation or hunger-related diseases every 10 seconds of the day.

Access to food constitutes a human right. In 1976, the United States Congress passed a Right to Food Resolution which declared the sense of the congress to be "that all people have a right to a nutritionally adequate diet". **Physicians Against World Hunger** (PAWH), a non-profit, tax-exempt organization was founded so that physicians could collectively defend this human right by raising funds to support well-recognized, reputable organizations that are directly engaged in working with the poor primarily for the purpose of ending death by starvation.

Please do not ignore this plea. On PAWH day—the third Tuesday in October—please donate your earnings to help end world hunger. It may be the single most important life-saving measure you will take that day. Please don't turn your back on your fellow man whose only fault was to have been born at the wrong time in the wrong place. Together physicians must help bring an end to this genocide.

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The Patient Self-Determination Act: Shared Decision Making in the Doctor-Patient Relationship

JOSEPH M. HEALEY, J.D.

IN its 1982 report, *Making Health Care Decisions*,[1] the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research reviewed the two dominant models of the patient-professional relationship, medical paternalism and patient sovereignty, and proposed a shift in emphasis toward a relationship characterized by mutual participation, respect, and shared decision making.[1(p36)]

In the period since that report, legal developments in the areas of consent to treatment, refusal of treatment, and advance directives have supported an increased role for patients within the professional-patient relationship and have contributed to an increasing acceptance of it by both professionals and patients. Most recently, a federal statute, The Patient Self-Determination Act (PSDA), continues this legal trend by requiring that patients be provided information about their rights under state law and under institutional and organizational policies. The PSDA provides an opportunity to reaffirm the shared decision making model of the professional-patient relationship.

The PSDA requires each hospital, nursing facility, provider of home health care or personal care services, hospice program, and health maintenance organization receiving funds under Medicare or Medicaid to maintain written policies and procedures concerning the individual's rights under state law to make decisions concerning medical care, including the right to accept or refuse treatment and the right to formulate advance directives. It also requires the institution, facility, or organization to distribute written information to all adult patients receiving care by or through the provider or organization about their rights and about implementation of their rights within the institution, facility, or organization. Among further obligations imposed is the requirement to document in the patient's medical record whether or not the individual has executed an advance directive.

Implementation of the PSDA provides an opportunity for the attending physician to encourage patients to consider how they would want decisions to be made if they became unable to make them for themselves and to consider taking a more active role in their health care decisions. Though the PSDA places the legal obligation to disclose information on the institution, facility, or organization, such efforts are unlikely to encourage patient involvement without the cooperation of the patient's attending physician. There are several ways that the attending physician can assist in this process.

First, for patients undergoing hospitalization, as part of pre-admission discussions with the patient, the attending physician should describe the material that the patient will receive and explain the opportunities available to the patient. Patients should be encouraged to consider the importance of clarifying their views with respect to health care decisions and with respect to the person they would choose to serve as proxy if they should be unable to make decisions for themselves. Second, the attending physician should encourage discussion about their wishes by the patient with other family members to avoid misunderstanding and lack of communication about these most important issues. Third, the attending physician should be able to refer patients to appropriate resources to clarify options, rights, and responsibilities.

One effect of this attention to advance directives should be increased emphasis on the rights and responsibilities of professionals and patients in a relationship characterized by mutual respect and shared decision making. In contrast to the medical paternalism model, patients are encouraged to know their rights and to assume responsibility for their health care decisions. In contrast to the patient sovereignty model, doctors are expected to serve as partners and not merely as the technically competent agents of the patient's wishes. The PSDA provides an opportunity to promote a model of the doctor-patient relationship consistent with trends so prominent during the past decade.

REFERENCE

1. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Making Health Care Decisions: The Ethical and Legal Implications of Informed Consent in the Patient-Practitioner Relationship, Volume One: Report.* Washington: U.S. Government Printing Office, 1982.

JOSEPH M. HEALEY, J.D., Professor, Department of Community Medicine and Health Care, University of Connecticut School of Medicine, Farmington, CT.

Letter to the Editor

Letters to the Editor are considered for publication (subject to editing and abridgment), provided that they are submitted in duplicate, signed by all authors, typewritten in double spacing, and do not exceed 1½ pages of text (excluding references). They should not duplicate similar material being submitted or published elsewhere. Letters referring to a recent *Journal* article should be received within six weeks of the article's publication.

WRITING EXERCISE PRESCRIPTIONS

To the Editor: Public awareness of the value of exercise to avoid vascular stagnation has created a profit windfall for advertisers and manufacturers of iron muscle-building machines. Although countless Miss Americas have fulfilled their exercise needs with fifteen minutes of calisthenics daily, such a little used costly and bulky "muscle-machine" could cramp a city apartment as a libation to the gods.

Excellent exercise programs are worked out in a time frame of three times a week. A prompter on the radio or TV, or a record or tape on a player may be all that is needed for ardent participation. The subject need only be convinced and instructed, and all this could well be done by his or her primary physician. It might be ideal for a physician to set the example.

Therapeutic exercise is already well established in musculoskeletal pathology,—what better cure than exercise is there for a frozen shoulder or painful back? (Perhaps a little "moist heat and ultrasound" help maintain timely supervision and resolve!) There is great medical gain in fighting off "couch potato" tendencies.

Writing exercise prescriptions is a skill any physician could well cultivate. Civilization has altered the natural environment, but it has not changed the way heart and brain and the liver and kidneys work. The microslide of a muscle biopsy of a well-exercised mouse shows three times the capillary bed of an immobilized one. What then might the macroscopic vascular bed of a well-exercised man show?

Sidney Vernon, M.D.

Willimantic

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MEDICAL NEWS CAPSULES

The Month's Reading in Review

TIMOTHY B. NORBECK

- Remember the public outrage last year over Senator Quentin Burdick's (ND) bill to appropriate $500,000 to restore Lawrence Welk's birthplace?...Apparently U.S. Representative Jim Slattery (Kansas) had introduced an amendment which would rescind Burdick's appropriations...Before the vote in the House, however, a member of Burdick's staff telephoned the dean of Kansas State University (which just happened to be in Slattery's district) and suggested that the university's $5.3 million grant application might have trouble getting past Burdick...Then North Dakota Representative Byron Dorgan warned that other "pork" headed for Kansas could be detoured...Slattery did prevail, but it is likely that his district will see a drying up of future government subsidies.
- Pork barrel projects emerging in 1992 for consideration by Congress:
  - a $94,000 study of "apple quality."
  - $1 million to determine why people don't use bicycles or walking "as a means of transportation."
  - $37,000 to develop comprehensive management technologies "for the handling of animal manure."
  - $80,000 to determine if floss from milkweed pods could replace goose down in bedding.
- There has been at least one physician member of every Congress since 1774...Current membership of the House of Representatives includes two physicians: Jim McDermott, (D-WA) and J. Roy Rowland, (D-GA)...Dr. Rowland has been in the forefront in pressing anti-hassle Medicare legislation.
- A recent Conference Board survey found that medical costs, the federal budget deficit, and unemployment are of increasing public concern...Taken in 5,000 representative households, the survey asked people to rank the seriousness of 22 economic and social problems...Almost nine out of ten agreed that the cost of medical care was "a most serious" or "serious" problem, putting it at the top of the list of 22...Closely following on the list were drug abuse, the budget deficit, crime, unemployment, and AIDS.
- *Business Week* reports that law firms that fattened up in the 1980s are hurting...Battered by the recession and an increasing number of cost-conscious clients, firms are deferring starting dates for new hires and even rescinding job offers...Top firms may start cutting the going rate for starting salaries which is now up to $85,000 per year...Since the mid-1980s, law schools have graduated 35,000 a year, and an unprecedented 94,000 applicants are competing to enter law school this fall.
- The U.S. currently spends 12.4% of its GNP on health care...According to Employee Benefit Research Institute (Washington, D.C.), 36% of employer funding for benefits went to health care in 1989, up from 23% in 1970...Health care now accounts for 5.8% of total compensation, up from 2.4% twenty years ago.
- As reported in *Reader's Digest*, the same group of farmers received $66 million from the Bureau of Reclamation and $379 million from the Department of Agriculture in 1986 (according to a Department of the Interior report)...What's wrong with that, one might ask?...Well, the $66 million was to pay them to irrigate land that produced surplus crops, while the $379 million was to pay them to limit surplus crops!
- According to the Omaha-based Wellness Councils of America, "Concrete proof now exists that wellness programs pay off in lower health care costs, reduced absenteeism, increased productivity, and higher morale"...The Travelers Corporation saved $7.8 million in employee benefit costs in 1990 by using a health promotion program...The savings represented a return of $3.40 for every $1 spent on the program.
- The Census Bureau reports that the poverty rate for persons over 65 climbed to 12.2% in 1990, up from 11.4% in 1989...An additional 295,00 persons over 65 fell below the poverty line of $6,268 a year for one person and $7,905 for two...For children 18 and under, the poverty rate was 20.6% in 1990, an increase from 19.6% in 1989.
- According to the *San Jose Mercury-News*, the chief executives of California's 10 largest counties will earn an average of $132,000 this year, which is about 48% more than they made five years ago...The voters of Pasadena thought that they had found a solution to that escalation by requiring the city council to get the approval of voters for any salary increases...But when those voters rejected an increase the council had recently given itself, the council countered with the ingenious move of raising the salaries of the members of the city's Development Commission...Those members of the Development Commission just happened to be the same people as on the city council!

TIMOTHY B. NORBECK is Executive Director of the Connecticut State Medical Society.

CSMS PHYSICIAN PLACEMENT SERVICE

The Society maintains the Physician Placement Service as a *free* service to the medical profession, hospitals, and communities in Connecticut.

Opportunities* should be typed, double-spaced copy on letterhead and submitted to CSMS, Physician Placement Service, 160 St. Ronan St., New Haven, CT 06511 (203)-865-0587. These will be published as space permits and will be distributed to physicians making inquiries of such *opportunities.

***Physicians wishing to locate* in Connecticut may call the office requesting opportunities in their specialty. Also, candidates are invited to submit a resume to be kept on file with the Society. An announcement of a physician's availability will be published in two issues of *Connecticut Medicine* as space permits.**

Listing of physicians in the Placement Service does not in any way represent certification by the Society. Investigation of credentials and experience is the responsibility of those seeking applicants for positions.

Announcements on the Physician Placement Service page under Classified Advertising are charged at the regular Classified Advertising rate.

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3. Influenza vaccine—recommendations of the Public Health Service Advisory Committee on Immunization Practices. *MMWR* 1979;28:231-8.
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